# EXHIBIT 7

US006329161B1

(12) **United States Patent**
**Heller et al.**

(10) **Patent No.: US 6,329,161 B1**
(45) **Date of Patent: Dec. 11, 2001**

(54) **SUBCUTANEOUS GLUCOSE ELECTRODE**

(75) Inventors: **Adam Heller**; **Michael V. Pishko**, both of Austin, TX (US)

(73) Assignee: **TheraSense, Inc.**, Alameda, CA (US)

( * ) Notice: Subject to any disclaimer, the term of this patent is extended or adjusted under 35 U.S.C. 154(b) by 0 days.

(21) Appl. No.: **09/668,221**

(22) Filed: **Sep. 22, 2000**

**Related U.S. Application Data**

(63) Continuation of application No. 09/477,053, filed on Jan. 3, 2000, which is a continuation of application No. 09/356,102, filed on Jul. 16, 1999, now Pat. No. 6,121,009, which is a continuation of application No. 08/767,110, filed on Dec. 4, 1996, which is a continuation-in-part of application No. 08/299,526, filed on Sep. 1, 1994, now Pat. No. 5,593,852, and a continuation-in-part of application No. 08/161,682, filed on Dec. 2, 1993, now Pat. No. 5,356,786.

(51) **Int. Cl.**[7] ..... **C12Q 1/54**; C12Q 1/28; C12Q 1/32

(52) **U.S. Cl.** ..... **435/14**; 435/28; 435/26; 435/24; 435/288; 435/291; 204/403; 204/157.1; 204/153.1

(58) **Field of Search** ..... 435/14, 28, 26, 435/24, 288, 291; 204/403, 157.15, 153.1

(56) **References Cited**

U.S. PATENT DOCUMENTS

| | | | |
|---|---|---|---|
| Re. 32,947 | 6/1989 | Dorner et al. | 435/14 |
| 3,260,656 | 7/1966 | Ross, Jr. | 435/14 |
| 3,653,841 | 4/1972 | Klein | 435/14 |
| 3,719,564 | 3/1973 | Lilly, Jr. et al. | 435/14 |
| 3,776,832 | 12/1973 | Oswin et al. | 435/14 |
| 3,837,339 | 9/1974 | Aisenberg et al. | 435/14 |
| 3,926,760 | 12/1975 | Allen et al. | 435/14 |
| 3,972,320 | 8/1976 | Kalman | 435/14 |
| 3,979,274 | 9/1976 | Newman | 435/14 |
| 4,008,717 | 2/1977 | Kowarski | 435/14 |
| 4,016,866 | 4/1977 | Lawton | 435/14 |

(List continued on next page.)

FOREIGN PATENT DOCUMENTS

| | | |
|---|---|---|
| 29 03 216 | 8/1979 | (DE) . |
| 227 029 A3 | 9/1985 | (DE) . |
| 3934299 | 10/1990 | (DE) . |
| 44 01 400 A1 | 7/1995 | (DE) . |
| 0 010 375 A1 | 4/1980 | (EP) . |

(List continued on next page.)

OTHER PUBLICATIONS

Abruna, H. D. et al., "Rectifying Interfaces Using Two–Layer Films of Electrochemically Polymerized Vinylpyridine and Vinylbipyridine Complexes of Ruthenium and Iron on Electrodes," *J. Am. Chem. Soc.*, 103(1): 1–5 (Jan. 14, 1981)

Abstract from Korf, J. et al., "Monitoring of Glucose and Lactate Using Microdialysis: Applications in Neonates and Rat Brain", *Developmental Neuroscience*, vol. 15, No. 3–5, pp. 240–46 (1993).

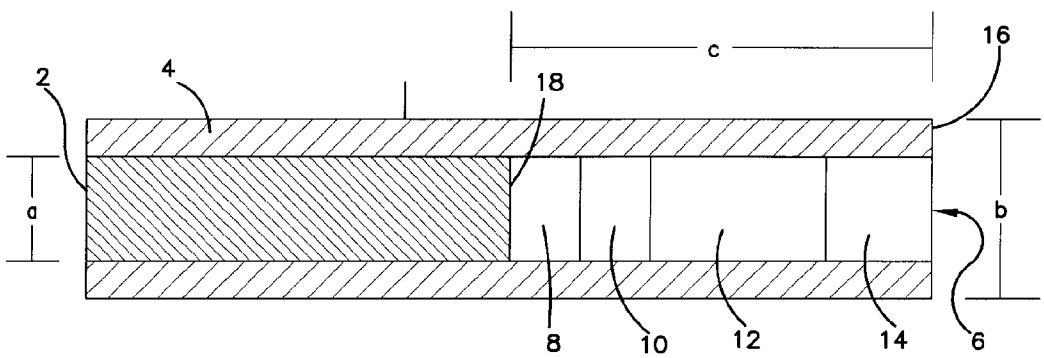
(List continued on next page.)

*Primary Examiner*—Louise N. Leary
(74) *Attorney, Agent, or Firm*—Merchant & Gould P.C.

(57) **ABSTRACT**

A small diameter flexible electrode designed for subcutaneous in vivo amperometric monitoring of glucoses is described. The electrode is designed to allow "one-point" in vivo calibration, i.e., to have zero output current at zero glucose concentration, even in the presence of other electroreactive species of serum or blood. The electrode is preferably three or four-layered, with the layers serially deposited within a recess upon the tip of a polyamide insulated gold wire. A first glucose concentration-to-current transducing layer is overcoated with an electrically insulating and glucose flux limiting layer (second layer) on which, optionally, an immobilized interference-eliminating horseradish peroxidase based film is deposited (third layer). An outer (fourth) layer is biocompatible.

**48 Claims, 10 Drawing Sheets**



U.S. PATENT DOCUMENTS


| | | | |
|---|---|---|---|
| 4,055,175 | 10/1977 | Clemens et al. | 435/14 |
| 4,059,406 | 11/1977 | Fleet | 435/14 |
| 4,076,596 | 2/1978 | Connery et al. | 435/14 |
| 4,098,574 | 7/1978 | Dappen | 435/14 |
| 4,100,048 | 7/1978 | Pompei et al. | 435/14 |
| 4,151,845 | 5/1979 | Clemens | 435/14 |
| 4,168,205 | 9/1979 | Danninger et al. | 435/14 |
| 4,172,770 | 10/1979 | Semersky et al. | 435/14 |
| 4,178,916 | 12/1979 | McNamara | 435/14 |
| 4,206,755 | 6/1980 | Klein | 435/14 |
| 4,224,125 | 9/1980 | Nakamura et al. | 435/14 |
| 4,240,438 | 12/1980 | Updike et al. | 435/14 |
| 4,247,297 | 1/1981 | Berti et al. | 435/14 |
| 4,340,458 | 7/1982 | Lerner et al. | 435/14 |
| 4,352,960 | 10/1982 | Dorner et al. | 435/14 |
| 4,356,074 | 10/1982 | Johnson | 435/14 |
| 4,365,637 | 12/1982 | Johnson | 435/14 |
| 4,366,033 | 12/1982 | Richter et al. | 435/14 |
| 4,375,399 | 3/1983 | Havas et al. | 435/14 |
| 4,384,586 | 5/1983 | Christiansen | 435/14 |
| 4,390,621 | 6/1983 | Bauer | 435/14 |
| 4,401,122 | 8/1983 | Clark, Jr. | 435/14 |
| 4,404,066 | 9/1983 | Johnson | 435/14 |
| 4,418,148 | 11/1983 | Oberhardt | 435/14 |
| 4,427,770 | 1/1984 | Chen et al. | 435/14 |
| 4,431,004 | 2/1984 | Bessman et al. | 435/14 |
| 4,436,094 | 3/1984 | Cerami | 435/14 |
| 4,440,175 | 4/1984 | Wilkins | 435/14 |
| 4,450,842 | 5/1984 | Zick et al. | 435/14 |
| 4,458,686 | 7/1984 | Clark, Jr. | 435/14 |
| 4,461,691 | 7/1984 | Frank | 435/14 |
| 4,469,110 | 9/1984 | Stama | 435/14 |
| 4,477,314 | 10/1984 | Richter et al. | 435/14 |
| 4,484,987 | 11/1984 | Gough | 435/14 |
| 4,522,690 | 6/1985 | Venkatasetty | 435/14 |
| 4,524,114 | 6/1985 | Samuels et al. | 435/14 |
| 4,526,661 | 7/1985 | Steckhan et al. | 435/14 |
| 4,534,356 | 8/1985 | Papadakis | 435/14 |
| 4,538,616 | 9/1985 | Rogoff | 435/14 |
| 4,543,955 | 10/1985 | Schroeppel | 435/14 |
| 4,545,382 | 10/1985 | Higgins et al. | 435/14 |
| 4,552,840 | 11/1985 | Riffer | 435/14 |
| 4,560,534 | 12/1985 | Kung et al. | 435/14 |
| 4,571,292 | 2/1986 | Liu et al. | 435/14 |
| 4,573,994 | 3/1986 | Fischell et al. | 435/14 |
| 4,581,336 | 4/1986 | Malloy et al. | 435/14 |
| 4,595,011 | 6/1986 | Phillips | 435/14 |
| 4,619,754 | 10/1986 | Niki et al. | 435/14 |
| 4,627,445 | 12/1986 | Garcia et al. | 435/14 |
| 4,627,908 | 12/1986 | Miller | 435/14 |
| 4,633,878 | 1/1987 | Bombardieri | 435/14 |
| 4,637,403 | 1/1987 | Garcia et al. | 435/14 |
| 4,650,547 | 3/1987 | Gough | 435/14 |
| 4,654,197 | 3/1987 | Lilja et al. | 435/14 |
| 4,655,880 | 4/1987 | Liu | 435/14 |
| 4,655,885 | 4/1987 | Hill et al. | 435/14 |
| 4,671,288 | 6/1987 | Gough | 435/14 |
| 4,679,562 | 7/1987 | Luksha | 435/14 |
| 4,680,268 | 7/1987 | Clark, Jr. | 435/14 |
| 4,682,602 | 7/1987 | Prohaska | 435/14 |
| 4,684,537 | 8/1987 | Graetzel et al. | 435/14 |
| 4,685,463 | 8/1987 | Williams | 435/14 |
| 4,703,756 | 11/1987 | Gough et al. | 435/14 |
| 4,711,245 | 12/1987 | Higgins et al. | 435/14 |
| 4,717,673 | 1/1988 | Wrighton et al. | 435/14 |
| 4,721,601 | 1/1988 | Wrighton et al. | 435/14 |
| 4,721,677 | 1/1988 | Clark, Jr. | 435/14 |
| 4,726,378 | 2/1988 | Kaplan | 435/14 |
| 4,726,716 | 2/1988 | McGuire | 435/14 |
| 4,757,022 | 7/1988 | Shults et al. | 435/14 |
| 4,758,323 | 7/1988 | Davis et al. | 435/14 |
| 4,759,371 | 7/1988 | Pranetzki | 435/14 |
| 4,759,828 | 7/1988 | Young et al. | 435/14 |
| 4,764,416 | 8/1988 | Ueyama et al. | 435/14 |
| 4,776,944 | 10/1988 | Janata et al. | 435/14 |
| 4,777,953 | 10/1988 | Ash et al. | 435/14 |
| 4,781,798 | 11/1988 | Gough | 435/14 |
| 4,784,736 | 11/1988 | Lonsdale et al. | 435/14 |
| 4,795,707 | 1/1989 | Niiyama et al. | 435/14 |
| 4,796,634 | 1/1989 | Huntsman et al. | 435/14 |
| 4,805,624 | 2/1989 | Yao et al. | 435/14 |
| 4,813,424 | 3/1989 | Wilkins | 435/14 |
| 4,815,469 | 3/1989 | Cohen et al. | 435/14 |
| 4,820,399 | 4/1989 | Senda et al. | 435/14 |
| 4,822,337 | 4/1989 | Newhouse et al. | 435/14 |
| 4,830,959 | 5/1989 | McNeil et al. | 435/14 |
| 4,832,797 | 5/1989 | Vadgama et al. | 435/14 |
| 4,840,893 | 6/1989 | Hill et al. | 435/14 |
| 4,848,351 | 7/1989 | Finch | 435/14 |
| 4,854,322 | 8/1989 | Ash et al. | 435/14 |
| 4,871,351 | 10/1989 | Feingold | 435/14 |
| 4,871,440 | 10/1989 | Nagata et al | 435/14 |
| 4,874,500 | 10/1989 | Madou et al. | 435/14 |
| 4,890,620 | 1/1990 | Gough | 435/14 |
| 4,894,137 | 1/1990 | Takizawa et al. | 435/14 |
| 4,897,162 | 1/1990 | Lewandowski et al | 435/14 |
| 4,897,173 | 1/1990 | Nankai et al. | 435/14 |
| 4,909,908 | 3/1990 | Ross et al. | 435/14 |
| 4,911,794 | 3/1990 | Parce et al. | 435/14 |
| 4,917,800 | 4/1990 | Lonsdale et al. | 435/28 |
| 4,919,141 | 4/1990 | Zier et al. | 435/28 |
| 4,919,767 | 4/1990 | Vadgama et al. | 435/28 |
| 4,923,586 | 5/1990 | Katayama et al. | 435/28 |
| 4,927,516 | 5/1990 | Yamaguchi et al. | 435/28 |
| 4,934,369 | 6/1990 | Maxwell | 435/28 |
| 4,935,105 | 6/1990 | Churchouse | 435/28 |
| 4,935,345 | 6/1990 | Guilbeau et al. | 435/28 |
| 4,938,860 | 7/1990 | Wogoman | 435/14 |
| 4,944,299 | 7/1990 | Silvian | 435/14 |
| 4,950,378 | 8/1990 | Nagata | 435/14 |
| 4,953,552 | 9/1990 | DeMarzo | 435/14 |
| 4,954,129 | 9/1990 | Giuliani et al. | 435/14 |
| 4,969,468 | 11/1990 | Byers et al. | 435/14 |
| 4,970,145 | 11/1990 | Bennetto et al. | 435/14 |
| 4,974,929 | 12/1990 | Curry | 435/14 |
| 4,986,271 | 1/1991 | Wilkins | 435/14 |
| 4,994,167 | 2/1991 | Shuls et al. | 435/14 |
| 5,001,054 | 3/1991 | Wagner | 435/14 |
| 5,002,054 | 3/1991 | Ash et al. | 435/14 |
| 5,058,592 | 10/1991 | Whisler | 435/14 |
| 5,070,535 | 12/1991 | Hochmair et al. | 435/14 |
| 5,082,550 | 1/1992 | Rishpon et al. | 435/14 |
| 5,082,786 | 1/1992 | Nakamoto | 435/14 |
| 5,089,112 | 2/1992 | Skotheim et al. | 435/14 |
| 5,095,904 | 3/1992 | Seligman et al. | 435/14 |
| 5,101,814 | 4/1992 | Palti | 435/14 |
| 5,106,365 | 4/1992 | Hernandez | 435/14 |
| 5,108,564 | 4/1992 | Szuminsky et al. | 435/14 |
| 5,109,850 | 5/1992 | Blanco et al. | 435/14 |
| 5,120,420 | 6/1992 | Nankai et al. | 435/14 |
| 5,126,034 | 6/1992 | Carter et al. | 435/14 |
| 5,133,856 | 7/1992 | Yamaguchi et al. | 435/14 |
| 5,135,003 | 8/1992 | Souma | 435/14 |
| 5,141,868 | 8/1992 | Shanks et al. | 435/14 |
| 5,161,532 | 11/1992 | Joseph | 435/14 |
| 5,165,407 | 11/1992 | Wilson et al. | 435/14 |
| 5,174,291 | 12/1992 | Schoonen et al. | 435/14 |
| 5,190,041 | 3/1993 | Palli | 435/14 |
| 5,192,416 | 3/1993 | Wang et al. | 435/14 |
| 5,198,367 | 3/1993 | Aizawa et al. | 435/14 |
| 5,202,261 | 4/1993 | Musho et al. | 435/14 |

| | | | | |
|---|---|---|---|---|
| 5,205,920 | | 4/1993 | Oyama et al. | 435/14 |
| 5,208,154 | | 5/1993 | Weaver et al. | 435/14 |
| 5,209,229 | | 5/1993 | Gilli | 435/14 |
| 5,217,595 | | 6/1993 | Smith et al. | 435/14 |
| 5,229,282 | | 7/1993 | Yoshioka et al. | 435/14 |
| 5,250,439 | | 10/1993 | Musho et al. | 435/14 |
| 5,262,035 | | 11/1993 | Gregg et al. | 435/14 |
| 5,262,305 | | 11/1993 | Heller et al. | 435/14 |
| 5,264,103 | | 11/1993 | Yoshioka et al. | 435/14 |
| 5,264,104 | | 11/1993 | Gregg et al. | 435/14 |
| 5,264,106 | | 11/1993 | McAleer et al. | 435/14 |
| 5,271,815 | | 12/1993 | Wong | 435/14 |
| 5,279,294 | | 1/1994 | Anderson et al. | 435/14 |
| 5,286,362 | | 2/1994 | Hoenes et al. | 435/14 |
| 5,286,364 | | 2/1994 | Yacynych et al. | 435/14 |
| 5,288,636 | | 2/1994 | Pollmann et al. | 435/14 |
| 5,293,546 | | 3/1994 | Tadros et al. | 435/14 |
| 5,320,098 | | 6/1994 | Davidson | 435/14 |
| 5,320,725 | | 6/1994 | Gregg et al. | 435/14 |
| 5,322,063 | | 6/1994 | Allen et al. | 435/14 |
| 5,337,747 | | 8/1994 | Neftel | 435/14 |
| 5,352,348 | | 10/1994 | Young et al. | 435/14 |
| 5,356,786 | * | 10/1994 | Heller et al. | 435/14 |
| 5,368,028 | | 11/1994 | Palti | 435/14 |
| 5,372,133 | | 12/1994 | Esch | 435/14 |
| 5,376,251 | | 12/1994 | Kaneko et al. | 435/14 |
| 5,378,628 | | 1/1995 | Gratzel et al. | 435/14 |
| 5,387,327 | | 2/1995 | Khan | 435/14 |
| 5,390,671 | | 2/1995 | Lord et al. | 435/14 |
| 5,391,250 | | 2/1995 | Cheney, II et al. | 435/14 |
| 5,395,504 | | 3/1995 | Saurer et al. | 435/14 |
| 5,411,647 | | 5/1995 | Johnson et al. . | |
| 5,437,999 | | 8/1995 | Diebold et al. . | |
| 5,462,645 | | 10/1995 | Albery et al. . | |
| 5,469,846 | | 11/1995 | Khan . | |
| 5,494,562 | | 2/1996 | Maley et al. . | |
| 5,496,453 | | 3/1996 | Uenoyama et al. . | |
| 5,497,772 | | 3/1996 | Schulman et al. . | |
| 5,531,878 | | 7/1996 | Vadgama et al. . | |
| 5,545,191 | | 8/1996 | Mann et al. . | |
| 5,560,357 | | 10/1996 | Faupel et al. | 435/14 |
| 5,565,085 | | 10/1996 | Ikeda et al. | 435/14 |
| 5,567,302 | | 10/1996 | Song et al. | 435/14 |
| 5,568,806 | | 10/1996 | Cheney, II et al. | 435/14 |
| 5,569,186 | | 10/1996 | Lord et al. | 435/14 |
| 5,582,184 | | 12/1996 | Erickson et al. | 435/14 |
| 5,582,697 | | 12/1996 | Ikeda et al. | 435/14 |
| 5,582,698 | | 12/1996 | Flaherry et al. | 435/14 |
| 5,586,553 | | 12/1996 | Halili et al. | 435/14 |
| 5,589,326 | | 12/1996 | Deng et al. | 435/14 |
| 5,593,852 | * | 1/1997 | Heller et al. | 435/14 |
| 5,596,150 | | 1/1997 | Arndt et al. | 435/14 |
| 5,617,851 | | 4/1997 | Lipkover | 435/14 |
| 5,628,890 | | 5/1997 | Carter et al. | 435/14 |
| 5,651,869 | | 7/1997 | Yoshioka et al. | 435/14 |
| 5,660,163 | | 8/1997 | Schuylman et al. | 435/14 |
| 5,670,031 | | 9/1997 | Hintsche et al. | 435/14 |
| 5,680,858 | | 10/1997 | Hansen et al. | 435/14 |
| 5,682,233 | | 10/1997 | Brinda | 435/14 |
| 5,695,623 | | 12/1997 | Michel et al. | 435/14 |
| 5,708,247 | | 1/1998 | McAleer et al. | 435/14 |
| 5,711,861 | | 1/1998 | Ward et al. | 435/14 |
| 5,711,862 | | 1/1998 | Sakoda et al. | 435/14 |
| 5,741,211 | | 4/1998 | Renirie et al. | 435/14 |
| 5,791,344 | | 8/1998 | Schulman et al. | 435/14 |
| 6,121,009 | * | 9/2000 | Heller et al. | 435/14 |

FOREIGN PATENT DOCUMENTS

| | | |
|---|---|---|
| 0 026 995 A1 | 4/1981 | (EP) . |
| 0 048 090 A2 | 3/1982 | (EP) . |
| 0 078 636 A1 | 5/1983 | (EP) . |
| 0 096 288 A1 | 12/1983 | (EP) . |
| 0 125 139 A2 | 11/1984 | (EP) . |
| 0 127 958 A2 | 12/1984 | (EP) . |
| 0 136 362 A1 | 4/1985 | (EP) . |
| 0 170 375 A2 | 2/1986 | (EP) . |
| 0 177 743 A2 | 4/1986 | (EP) . |
| 0 080 304 B1 | 5/1986 | (EP) . |
| 0 184 909 A2 | 6/1986 | (EP) . |
| 0 206 218 A2 | 12/1986 | (EP) . |
| 0 230 472 A1 | 8/1987 | (EP) . |
| 0 241 309 A3 | 10/1987 | (EP) . |
| 0 245 073 A2 | 11/1987 | (EP) . |
| 0 278 647 A2 | 8/1988 | (EP) . |
| 0 359 831 A2 | 3/1990 | (EP) . |
| 0 368 209 A1 | 5/1990 | (EP) . |
| 0 390 390 A1 | 10/1990 | (EP) . |
| 0 400 918 A1 | 12/1990 | (EP) . |
| 0 453 283 A1 | 10/1991 | (EP) . |
| 0 470 290 A1 | 2/1992 | (EP) . |
| 0 127 958 B2 | 3/1992 | (EP) . |
| 0 255 291 B1 | 6/1992 | (EP) . |
| 1394171 | 5/1975 | (GB) . |
| 1599241 A | 9/1981 | (GB) . |
| 2 073 891 A | 10/1981 | (GB) . |
| 2 154 003 B | 2/1988 | (GB) . |
| 2 204 408 A | 11/1988 | (GB) . |
| 2 254 436 A | 10/1992 | (GB) . |
| 54-41191 | 4/1979 | (JP) . |
| 55-10581 | 1/1980 | (JP) . |
| 55-10583 | 1/1980 | (JP) . |
| 55-10584 | 1/1980 | (JP) . |
| 55-12406 | 1/1980 | (JP) . |
| 56-163447 | 12/1981 | (JP) . |
| 60-173457 | 9/1985 | (JP) . |
| 60-173458 | 9/1985 | (JP) . |
| 60-173459 | 9/1985 | (JP) . |
| 61-90050 | 5/1986 | (JP) . |
| 62-85855 | 4/1987 | (JP) . |
| 62-114747 | 5/1987 | (JP) . |
| 63-58149 | 3/1988 | (JP) . |
| 57-70448 | 4/1988 | (JP) . |
| 63-128252 | 5/1988 | (JP) . |
| 63-139246 | 6/1988 | (JP) . |
| 63-294799 | 12/1988 | (JP) . |
| 63-317757 | 12/1988 | (JP) . |
| 63-317758 | 12/1988 | (JP) . |
| 1-114746 | 5/1989 | (JP) . |
| 1-114747 | 5/1989 | (JP) . |
| 1-124060 | 5/1989 | (JP) . |
| 1-134244 | 5/1989 | (JP) . |
| 1-156658 | 6/1989 | (JP) . |
| 2-62958 | 3/1990 | (JP) . |
| 2-120655 | 5/1990 | (JP) . |
| 2-287145 | 11/1990 | (JP) . |
| 2-310457 | 12/1990 | (JP) . |
| 3-26956 | 2/1991 | (JP) . |
| 3-28752 | 2/1991 | (JP) . |
| 3-202764 | 9/1991 | (JP) . |
| 5-72171 | 3/1993 | (JP) . |
| 5-196595 | 8/1993 | (JP) . |
| 6-190050 | 7/1994 | (JP) . |
| 7-72585 | 3/1995 | (JP) . |
| 1281988 A1 | 1/1987 | (SU) . |
| WO 85/05199 | 11/1985 | (WO) . |
| WO 89/08713 | 9/1989 | (WO) . |
| WO 90/05300 | 5/1990 | (WO) . |
| WO 90/05910 | 5/1990 | (WO) . |
| WO 91/01680 | 2/1991 | (WO) . |
| WO 91/04704 | 4/1991 | (WO) . |
| WO 91/15993 | 10/1991 | (WO) . |
| WO 92/13271 | 8/1992 | (WO) . |

| | | |
|---|---|---|
| WO 94/20602 | 9/1994 | (WO) . |
| WO 94/27140 | 11/1994 | (WO) . |
| WO 96/30431 | 10/1996 | (WO) . |
| WO 97/02847 | 1/1997 | (WO) . |
| WO 97/19344 | 5/1997 | (WO) . |
| WO 97/42882 | 11/1997 | (WO) . |
| WO 97/42883 | 11/1997 | (WO) . |
| WO 97/42886 | 11/1997 | (WO) . |
| WO 97/42888 | 11/1997 | (WO) . |
| WO 97/43962 | 11/1997 | (WO) . |

OTHER PUBLICATIONS

Aisenberg et al., "Blood glucose, level monitoring alarm system," Great Britain Patent GB 1394171, issued May 14, 1975. (Abstract only).

Albery, W. J. et al., "Amperometric Enzyme Electrodes," *Phil. Trans. R. Soc. Lond.*B316:107–119 (1987).

Albery, W. J. et al., "Amperometric enzyme electrodes. Part II. Conducting salts as electrode materials for the oxidation of glucose oxidase," *J. Electroanal Chem. Interfacial Electrochem.*, 194(2) (1 page–Abstract only) (1985).

Alcock et al., "Continuous Analyte Monitorning in Aid Clinical Practice," *IEEE Engineering in Medicine and Biology*, pp. 319–325 (Jun./Jul. 1994).

Anderson, L. B. et al., "Thin–Layer Electrochemistry: Steady–State Methods fo Studying Rate Processes, " *J. Electroanal. Chem.*, 10:295–395 (1965).

Bartlett, P. N. et al., "Covalent Binding of Electron Relays to Glucose Oxidation," *J. Chem. Commun.*, 1603–1604 (1987).

Bartlett, P. N. et al., "Modification of glucose oxidase by tetrathiafulvalene," *J. Chem. Soc. Chem. Commun.*16(1 page –Abstract only) (1990).

Bartlett, P. N. et al., "Strategies for the Development of Amperometric Enzyme Electrodes." *Biosensors*. 3 359–379 (1987/1988).

Bindra, D. S. et al., "Design and in Vitro Studies of a Needle–Type Glucose Sensor for Subcutaneous Monitoring", *Anal. Chem.*, 63(17): 1692–1696 (Sep. 1, 1991).

Bobbioni–Harsch et al., "Lifespan of subcutaneous glucose sensors and their performances during dynamic glycaemia changes in rats," *J. Biomed. Eng.*, vol. 15, pp. 457–463 (Nov. 1993).

Brandt, J. et al., "Covalent attachment of proteins to polysaccharide carriers by means of benzoqinone," *Biochim. Biophys. Acta.*386(1) (1 page Abstract only) (1975).

Brownlee, M. et al., "A Glucose–Controlled Insulin–Delivery System: Semisynthetic Insulin Bound to Lectin", *Science*, 206(4423): 1190–1191 (Dec. 7, 1979).

Cass, A. E. G. et al., "Ferrocene–Mediated Enzyme Electrode for Amperometric Determination of Glucose", *Anal. Chem*, 56(4): 667–671 (Apr. 1984).

Cass, A. E. G. et al., "Ferricinum Ion As An Electron Acceptor for Oxido–Reductases," *J. Electroanal Chem.*, 190;117–127 (1985).

Csöregi, E. et al., "Design and Optimization of a Selective Subcutaneously Implantable Glucose Electrode Based on "Wired"Glucose Oxidase," *Anal. Chem.*67(7):1240–1241 (Apr. 1, 1995).

Castner, J. F. et al., "Mass Transport and Reaction Kinetic Parameters Determined Electrochemically for Immobilized Glucose Oxidase," *Biochemistry*, 23(10): 2203–2210 (1984).

Cerami, "Monitor for continuous in vivo measurement of glucose concentration," United States Patent 4,436,004, issued Mar. 13, 1984, 2 pages (Abstract only).

Claremeont, D.J. et al., "Biosensors for Continuous In Vivo Glucose Monitoring", *IEEE Engineering in Medicine and Biology Society 10th Annual International Conference*, New Orleans, Louisiana, 3 pages. (Nov. 4–7, 1988).

Clark, L.C., Jr. et al., "Electrode Systems for Continuous Monitoring in Cardiovascular Surgery," *Annals New York Academy of Sciences*, pp. 29–45 (1982).

Clark, L.C. et al., "Differential Anodic Enzyme Polarography for the Measurement of Glucose", *Oxygen Transport to Tissue: Instrumentation, Methods, and Physiology*, 127–132 (1973).

Clark, L.C. et al., "Long term Stability of Electroenzymatic Glucose Sensors Implanted in Mice," *Trans Am. Soc. Artif. Intern. Organs.*XXXIV:259–265 (1988).

Clarke, W. L., et al., "Evaluating Clinical Accuracy of Systems for Self–Monitoring of Blood Glucose," *Diabetes Care* 10(5): 622–628 (Sep.–Oct. 1987).

Csöregi, E. et al. "Design, Characterization and One–Point in Vivo Calibration in a Subcutaneously Implanted Glucose Electrode," *Anal. Chem.*66(19):3131–3138 (Oct. 1, 1994).

Csöregi, E. et al., "Design and Optimization of a Selective Subcutaneously Implantable Glucose Electrode Based on "Wired"Glucose Oxidase," *Anal. Chem.*67(7): 1240–1244 (Apr. 1, 1995).

Csöregi, E. et al., "On–Line Glucose Monitoring by Using Microdialysis Sampling and Amperometric Detection Based on "Wired"Glucose Oxidase in Carbon Paste," *Mikrochim. Acta*121:31–40 (1995).

Davis, G., "Electrochemical Techniques for the Development of Amperometric Biosensors", *Biosensors*, 1:161–178 (1985).

Degani, Y. et al., "Direct Electrical Communication between Chemically Modified Enzymes and Metal Electrodes. 1. Electron Transfer From Glucose Oxidase to Metal Electrodes via Electron Relays. Bound Covalently to the Enzyme," *J. Phys. Chem.*, 91(6): 1285–1289 (1987).

Degani, Y. et al., "Direct Electrical Communication between Chemically Modified Enzymes and Metal Electrodes. 2. Methods for Bonding Electron–Transfer Relays to Glucose Oxidase and D–Amino–Acid Oxidase," *J. Am. Chem. Soc.*, 110(8): 2615–2620 (1988).

Degani, Y. et al. "Electrical Communcation between Redox Centers of Glucose Oxidase and Electrodes via Electrostatically and Covalently Bound Redox Polymers, " *J. Am. Chem. Soc.*, 111:2357–2358 (1989).

Denisevich, P. et al., "Unidirectional Current Flow and Charge State Trapping at Redox Polymer Interfaces on Bilayer Electrodes: Principles, Experimental Demonstration, and Theory," *J. Am. Chem. Soc.*, 103(16):4727–4737 (1981).

Dicks, J. M., "Ferrocene modified polypyrrole with immobilised glucose oxidase and its application in amperometric glucose microbiosensors," *Ann. Biol. Clin.*, 47:607–619 (1989).

Ellis, C. D., "Selectivity and Directed Charge Transfer through an Electroactive Metallopolymer Film, " *J. Am. Chem. Soc.*103(25): 7480–7483 (1981).

Engstrom, R.C., "Electrochemical Pretreatment of Glassy Carbon Electrodes," *Anal. Chem.*, 54(13): 2310–2314 (Nov. 1982).

Engstrom, R.C. et al., "Characterization of Electrochemically Pretreated Glassy Carbon Electrodes", *Anal. Chem.*, 56(2): 136–141 (Feb. 1984).

Feldman, B.J. et al., "Electron Transfer Kinetics at Redox Polymer/Solution Interaces Using Microelectrodes and Twin Electrode Thin Layer Cells", *J. Electroanal. Chem.*, 194(1):63–81 (Oct. 10, 1985).

Fischer, H. et al., "Intramolecular Electron Transfer Mediated by 4,4'–Biyridine and Related Bridging Groups" *J. Am. Chem. Soc.*, 98(18):5512–5517 (Sep. 1, 1976).

Flentge, F. et al., "An Enzyme–Reactor for Electrochemical Monitoring of Choline and Acetylcholine: Applications in High–Performance Liquid Chromatrography, Drain Tissue, Microdialysis and Cerebrospinal Fluid", *Analytical Biochemistry*, vol. 204, No. 2, pp. 305–310 (Aug. 1, 1992).

Foulds, N.C. et al., "Enzyme Entrapment in Electrically Conducting Polymers, " *J. Chem. Soc., Parady Trans. J.*, 82:1259–1264 (1986).

Foulds, N.C. et al., "Immobilization of Glucose Oxidase in Ferrocene–Modified Pyrrole Polymers," *Anal. Chem.*60(22):2473–2478 (Nov. 15, 1988).

Franetzki, "Implantable, calibrateable measuring instrument for a body substance and a calibrating method," United States Patent 4,759,371, issue Jul. 26, 1988, 2 pages (Abstract only).

Frew, J.E. et al., "Electron–Transfer Biosensors", *Phil Trans. R. Soc. Lond.*, B316:95–106 (1987).

Gilli, "Apparatus and method employing plural electrode configurations for cardioversi on atrial fibrillation in an arrhythmia control system,", United States Patent 5,209,229, issued May 11, 1993, 2 pages (Abstract only).

Gordon, L. et al., "Selective detection in flow analysis based on the combination of immobilized enzymes and chemically modified electrodes, " *Analytical Chimica Acta.*, 250:203–248 (1991).

Gregg, B. A. et al., "Cross–Linked Redox Gels Containing Oxidase for Amperometric Biosensor Applications", *Analytical Chemistry*, 62(3):258–265 (Feb. 1, 1990).

Gregg, B. A. et al., "Redox Polymer Films Containing Enzymes. 1. A Redox–Conducting Epoxy Cement: Synthesis, Characterization, and Electrocatalytic Oxidation of Hydroquinone, " *J. Phys. Chem.*, 95(15):5970–5975 (1991).

Hale, P.D. et al., "A New Class of Amperometric Biosensor Incorporating a Polymeric Electron–Transfer Mediator," *J. Am. Chem. Soc.*, 111(9):3482–3484 (1989).

Harrison, D.J. et al., "Characterization of Perfluorosulfonic Acid Polymer Coated Enzyme Electrodes and a Miniaturized Integrated Potentiostat for Glucose Analysis in Whole Blood", *Anal. Chem.*, 60(19):2002–2007 (Oct. 1, 1988).

Hawkbridge, F. M. et al., "Indirect Coulomietric Titration of Biological Electron Transport Components, " *Analytical Chemistry*, 45(7):1021–1027 (Jun. 1973).

Heller, A., "Amperometric Insensors based on three–dimensionaal hydrogel–forming epoxy networks, " *Sensors and Actuators*, 13–14:180–183 (1993).

Heller, A., "Electrical Connection of Enzyme Redox Centers to Electrodes," *J. Phys. Chem.*, 96(9):3579–3587 (1992).

Ianniello, R.M. et al., "Differential Pulse Voltammetric Study of Direct Electron Transfer in Glucose Oxidase Chemically Modified Graphite Electrodes", *Anal. Chem.*, 54:(7):1098–1101 (Jun. 1981).

Ianniello, R.M. et al., "Immobilized Enzyme Chemically Modified Electrod as an Amperometric Sensor", *Anal. Chem.*, 53(13):2090–2095 (Nov. 1981).

Ikeda, T. et al., "Kinetics of Outer–Sphere Electron Transfers Between Metal Complexes in Solutions and Polymeric Films on Modified Electrodes", *J. Am. Chem. Soc.*, 103(25):7422–7425 (Dec. 16, 1981).

Ikeda, T. et al., "Glucose oxidase–immobilized benzoquinone–carbon paste electrode as a glucose sensor," *Agric. Biol. Chem.*, 49(2) (1 page –Abstract only)1985).

Johnson, J. M. et al., "Potential–Dependent Enzymatic Activity in an Enzyme Thin–Layer Cell." *Anal. Chem.*54: 1377–1383 91983):

Johnson K. W., "Reproducible Electrodeposition of Biomolecules for the Fabrication of Miniature Electroenzymatic Biosensors", *Sensors and Actuators & Chemical*, B5:85–89 (1991).

Jönsson, G. et al., "An Amperometric Glucose Sensor Made by Modification of a Graphite Electrode Surface With Immobilized Glucose Oxidase and Adsorbed Mediator", *Biosensors*, 1:355–368 (1985).

Josowicz, M. et al., "Electrochemical Pretreatment of Thin Film Platinum Electrodes", *J. Electrochem. Soc.*, 135(1): 112–115 (January 1988).

Katakis, I. et al., "Lα–Glycerophosphate and L–Lactate Electrodes Based on the Electrochemical "Wiring"of Oxidases, " *Analytical Chemistry*, 64(9): 1008–1013 (May 1, 1992).

Katakis, I. et al. "Electrostatic Control of the Electron Transfer Enabling Binding of Recombinant Glucose Oxidase and Redox Polyelectrolytes," *J. Am. Chem. Soc.*, 116(8):3617–3618 (1994).

Kenausis, G. et al., "Wiring of glucose oxidase and lactate oxidase within a hydrogel made with poly(vinyl pyridine) complexed with $[Os(4,4\text{–domethoxy–2,2–bipyridine})_2\text{-}C1]^{+/2+}$, " *J. Chem. Soc., Faraday Trans.*92(20):4131–4136 (1996).

Klein, "Method and apparatus for the control and regulation of glycemia," U.S. Patent 4,206,755, issued Jun. 10, 1980, 2 pages (Abstract only).

Klein, "Control and regulation device for glycemia, " Great Britain Patent 1599241A, issued Sep. 30, 1981 (Abstract only).

Koudelka, M. et al., "In–Vivo Behaviour of Hypodermically Implanted Microfabricated Glcusoe Sensors", *Biosensors & Bioelectronics*, 6(1):31–36 (1991).

Kulys, J. et al., "Mediatorless peroxidase electrode and preparation of bioenzyme sensors," *Bioelectrochemistry and Bioelectronics*, 6(1):31–36 (1990).

Lager, W. et al., "Implantable Electrocatalytic Glucose Sensor," *Horm. Metab. Res.*, 26: 526–530 (November 1994).

Laurell, T., "A Continuous Glucose Monitoring System Based on Microdialysis", *Journal of Med Eng. & Tech.*, vol. 16, No. 5, pp. 187–193 (September/October 1992).

Lawton, "Implantable electrochemical sensor," U.S. Patent 4,016,866 issued Apr. 12, 1977 2 pages (Abstract only).

Lindner, E. et al. "Flexible (Kapton–Based) Microsensor Arrays of High Stability for Cardiovascular Applications", *J. Chem. Soc. Faraday Trans.*, 89(2):361–367 (Jan. 21, 1993).

Maidan, R. et al. "Eliminatio of Electrooxidizabel Interferon–Produced Currents in Amperometric Biosensors," *Analytical Chemistry*, 64(23):2889–2896 (Dec. 1, 1992).

Marko–Varga, G. et al., "Enzyme–Based Biosensor as a Selective Detection Unit in Column Liquid Chromatography", *Journal of Chromatography*, vol. 660, pp. 153–167 (1994).

Mastrololaro, J.J. et al., "An Electroenzymatic Glucose Sensor Fabricated on a Flexible Substrate", *Sensors and Biosensors B Chemicals*, B5:139–144 (1991).

McNeil, C. J. et al., "Thermostable Reduced Nicotinamide Aenine Dinucleotide Oxidase: Application to Amperometric Enzyme Assay," *Anal. Chem.*, 61(1).25–29 (1989),.

Miyawaki, O. et al., "Electrochemical and Glucose Oxidase Coenzyme Activity of Flaven Adenine Dinucleotide Covalently Attached to Glassy Carbon at the Adenine Amino Group," *Biochimica et Biophysica Acta*, 838:60–68 (1985).

Moati–Sirat, D. et al., "Towards continuous glucose monitoring: in vivo evaluation of a miniaturized glucose sensor impolanted for several days in a rat subcutaneous tissue,"(1 page–Abstract only) *Diabetologia*35(3): 224–30 (March 1992).

Moati–Sirat, D. et al., "Evaluating in vitro and in vivo the interference of ascorbate and acetaminophen on glucose detection by a needle–type glucose sensor," *Biosensors & Bioelectronics*, 7(5):345–352 (1992).

Nagy, G. et al., "A New Type of Enzyme Electrode: The Acorbic Acid Eliminator Electrode,", *Life Sciences*, 31(23): 2611–2616 (1982).

Nakamura, S. et al., "Effect of Periodate Oxidation on the Structure and Properties of Glucose Oxidase, " *Biochimica et Biophysica Acta.*, 445:294–308 (1976).

Narazimhan, K. et al., p–Benzoquinone activation of metal oxide electrodes for attachment of enzymes, *Enzyme Microb. Technol.*, 7(6): 1 page –Abstract only) (1985).

Ohara, T. J. et al., "Glucose Electrodes Based on Cross–Linked $[Os(bpy)_2Cl]^{+/2+}$Complexed Poly (l–vinylimadazole) Films," *Analytical Chemistry*, 65(23):3512–3516 (Dec. 1, 1993).

Ohara, T. J. et al., ""Wired"Electrodes for Amperometric Determination of Glucuse or Lactate in the Presence of Intefering Substances," *Analytical Chemistry*, 66(15): 2451–2457 (Aug. 1, 1994).

Oharta, T. J., "Osmium Bipyridyl Redox Polymers Used in Enzyme Electrodes," *Platinum Metals Rev.*, 39(2):54–62 (April 1995).

Olievier, C. N. et al. "In vivo Measurement of Carbon Dioxide Tension with a Miniature Electrode," *Pfluger Arch*, 373. 269–272 (1978).

Paddock, R. et al., "Electrocatalytic reduction of hydrogen peroxide via direct electron transfer from pyrolytic graphite electrodes to irreversibgle adsorbed cytochrome c peroxidase," *J. Electroanal. Chem.*, 260:487–194 (1989).

Palleschi, G. et al. "A Study of Interferences in Glucose Measurements in Blood by Hydrogen Peroxide Based Gelucose Probes", *Anal. Biochem.*, 159:114–121 (1986).

Pankratov, i. et al. "Sol–gel derived renewable–surface biosensors," *Journal of Electroanalytical Chemistry*, 393:35–41 (1995).

Pathak, C. P. et al., "Rapid Photopolymerization of immunoprotective Gels in Contact with Cells and Tissue, " *J. Am. Chem. Soc.*, 114(21): 8311–8312 (1992).

Pickup, J. "Developing glucose sensors for in vivo use," *TIBTECII*, vol. 11, pp. 285–289 (July 1993).

Pickup, J. et al., "Potentially–implantable, amperometric glucose sensors with meidated electron transfer: improving the operating stability," *Biosensors*, 4(2), 109–19, (Abstract only) (1989).

Pickup, J. C. et al., "In vivo molecular sensing in diabetes mellitus: an implantable glucose sensor with direct electron transfer," *Diabetologia*, 32(3): 213–217 (1989).

Pishko, M. V. et al., "Amperometric Glucose Microelectrodes Prepared Through Immobilization of Glucose Oxidase in Redox Hydrogels", *Anal. Chem.*, 63(20):2268–2272 (Oct. 15, 1991).

Poitout, V., et al. "In vitro and in vivo evaluation in dogs of a miniaturized glucose sensor,"*ASAIO Transactions*, 37(3) (1 page Abstract only) (July–September 1991).

Poitout, V ET AL., "Calibration in dogs of subcutaneous miniaturized glucose sensor using a glucose meter for blood glucose determination," *Biosensors & Bioelectronics*, 7, pp. 587–592 (1992).

Poitout, V. et al., "A glucose monitoring system for on line estimation in man of blood glucose concentration using a miniaturezed glucose sensor implanted in the subcutaneous tissue and a wearable control unit." (1 page –Abstract only) *Diabetologia*36(7):658–63 (Hykt 1993).

Pollak, A., et al., "Enzyme Immobilization by Condensation Copolymerization into Cross–Linked Polyacrylamide Gels," *J. Am. Chem. Soc.*102(20):6324–6330 (1980).

Reach, G. et al., "Can Continuous Glucose Monitoring Be Used for the Treamtnt of Diabetes" *Analytical Chemistry*, 64(6).381–386 (Mar. 15, 1992).

Rebrin, K. et al., "Automated Feedback Control of Subcutaneous Glucose Concentration in Diabetic Dogs", *Diabetologia*, 32(8):573–576 (August 1989).

Sakakida, M. et al., "Ferrocene–mediate needle–type glucose sensor covered with newly designed biocompatible membrane." *Sensors and Actuators B*, 13–14:319–322 (1993).

Samuels, G. J. et al., "An Electrode–Supported Oxidation Catalyst Based on Ruthenium (IV) pH "Encapsulation"in a Polymer Film." *J. Am. Chem. Soc.*, 103(2):307–312 (1981).

Sasso, S.V. et al., "Electropolymerized 1,2–Diaminobenzene as a Means to Prevent Interferences and Fouling and Stabilize Immobilized Enzyme in Electrochemical Biosensors", *Anal. Chem.*, 62(1): 1111–1117 (Jun. 1, 1990).

Scheller, F. et al., "Enzyme electrodes and their application," *Phil. Trans. R. Soc. Lond.*, B 316. 85–94 (1987).

Schmehl, R.H. et al., "The Effect of Redox Site Concentration on the Rate of Mediated Oxidation of Solution Substrates by a Redox Copolymer Film", *J. Electroanal. Chem.*, 152:97–109 (Aug. 25, 1983).

Schmidt, F.J. et al., "Calibration of a Wearable Glucose Sensor", *The International Journal of Artificial Organs*, vol. 15 No. 1, pp. 55–61 (1992).

Shichiri, M. et al., "Glycaemic Control in Pancreatotomized Dogs with a Wearable Artificial Endocrine Pancreas", *Diabetologia*, 24(3): 179–184 (March 1983).

Sitampalam, G. et al., "Surface–Modified Electrochemical Detector for Liquid Chromatography", *Anal. Chem.*55(9):1608–1610 (August 1983).

Soegijoko, S. et al., *Horm. Metab. Res., Suppl. Ser.*, 12, pp. 165–169 (1982) (Abstract).

Sprules, S. D. et al., "Evaluation of a New Disposable Screen–Printed Sensor Strip for the Measurement of NADH and Its Modification to Produce a Lactate Biosensor Employing Microliter Volumes, " *Electroanalysis*, 8(6):539–543 (1996).

Stemberg, F. et al. "Calibration Problems of Subcutaneous Glucosensors when Applied "In–Situ"in Man." *Horm. metabl. Res.*26.524–525 (1994).

Sternberg, R. et al., "Covalent Enzyme Coupling on Cellulose Acetate Membranesw for Glucose Sensor Development," *Analytical Chemistry*, 60(24):2781–2786 (Dec. 15, 1988).
Sternberg, R. et al., "Study and Development of Multilayer Needle–type Enzyme–based Glucose Microsensors," *Biosensors*, 4:27–40 (1988).
Suekane, M., "Immobiization of glucose isomerase," *Zeitschrift für Allgemeine Mikrobiologie*, 22(8):565–576 (1982).
Tajima, S. et al., "Simultaneous Determination of Glucose and 1,5–Anydroglucitol", *Chemcal Abstracts*, 111(25):394 111:228556g (Dec. 18, 1989).
Tarasevbich, M.R. "Bioelectrocatalysis", *Comprehensive Treatise of Electrofhemistry*, 10 (Ch. 4) 231–295 (1985).
Tatsuma, T. et al., "Enzyme Monolayer–and Bilayer–Modified Tin Oxide Electroes for the Determination of Hydrogen Peroxide and Glucose, " Anal. Chem. 61(21);2352–2355 (Nov. 1, 1989).
Taylor, C. et al., "Wiring of glcuose oxidase within a hydrogel made withy polyvinyl imidazole complexed with [(Os 4,4'–dimethoxy–,2–bipyridine)C1]+/2 +, " Journal of Electroanalytical Chemistry, 396:511–515 (1995).
Trojanowicz, M. et al., "Enzyme Entrapped Polypyrrole Modified Electrode for Flow–Injection Determination of Glucose," *Biosensors & Bielectronics*, 5:149–156 (1990).
Turner, A.P.F. et al., "Diabetes Mellitus; Biosensors for Research and Management", *Biosensors*, 1:85–115 (1985).
Turner, R. F. B. et al., "A Biocompatible Enzyme Electrode for Continuous in vio Glucose Monitoring in Whole Blood," *Sensors and Actuators*, B1 (1–6): 56–564 (January 1990).
Tuzhi, P. et al., "Constant Potential Pretreatment of Carbon Fiber Electrodes for In Vivo Electrochemistry", *Analytical Letters*, 24(6): 935–945 (1991).
Umaha, M., "Protein–Modified Electrochemically Active Biomaterial Surface", *U.S. Army Research Office Report*, (12 pages) (December 1988).
Urban, G. et al., "Miniaturized Thin–Film Biosensors Using Covalently Immobilized Glucose Oxidase," *Biosensors & Bioelectronics*, 6(7): 555–562 (1991).
Vadgama et al., "Sensor devices, " U.S. Patent 5,531,878, issued Jul. 2, 1996, 2 pages (Abstract only).
Velho et al., "Strategies for calibrating a subcutaneous glucose sensor," *Biomedica Biochimica Acta*.vol. 48, Issue 11–12, pp. 957–964 (1989).
Velho, G. et al., "In Vitro and In Vivo Stability of Electrode Potentials in Needle–Type Glucose Sensors", *Diabetes*, 38(2) 164–171 (February 1989).
Vreeke, M. et al., "Hydrogen Peroxide and β–Nicotinamide Adenine Dincucleotide Sensing Amperometric Electrodes Based on Electrical Connection of Horseradish Peroxidase Redox Centers to Electrodes through a Three–Dimensional Electron Relaying Polymer Network", *Analytical Chemistry*, 64(24):3084–3090 (Dec. 15, 1992).
Vrecke, M. S. et al., "Chapter 15: Hydrogen Peroxide Electrodes Based on Electrical Connection of Redox Centers of Various Peroxidases to Electrodes through a Three–Dimensional Electron–Relaying Polymer Network," *Diagnostic Biosensor Polymers*, 7 pages (July 26, 1993).
Wang, D. L. et al., "Miniaturized Flexible Amperometric Lactate Probe," *Analytical Chemistry*, 65(8):1069–1073 (Apr. 15, 1993).
Wang, J. et al., "Activation of Glassy Carbon Electrodes by Alternating Current Electrochemical Treatment," *Analytical Chimica Acta*, 167:325–334 (January 1985).
Wang, J. et al., "Amperometric biosensing of organic peroxides with peroxidase–modified electrodes," *Analytica Chimica Acta*254:81–88 (1991).
Wang, J. et al., "Screen–Printable Sol–Gel Enzyme–Containing Carbon links," *Analytical Chemistry*, 68(15). 275–2708 (Aug. 1, 1996).
Wang, J. et al., "Sol–Gel Derived Metal–Dispersed Carbon Composite Amperometric Biosensors," *Electronalysis*, 9(1):52–53 (1997).
Wiliams, D. L. et al., "Electrochemical–Enzymatic Analysis of Blod Glucose and Lactate," *Anal Chem*, 42(1): 118–121 (January 1970).
Wilson G. S. et al., "Progress toward the Development of an Implantable Sensor for Glucose," *Clinical Chemistry*, 38(9): 161391617 (1992).
Yabuki, S. et al., "Electro–conductive Enzyme Membrane," *J. Chem. Soc. Chem. Commun.*, 945–946 (1989).
Yang, L. et al., "Determination of Oxidase Enzyme Substrate Using Cross–Flow Thin–Layer Amperometry," *Electroanalysis*, 8(8–9):716–721 (1996).
Yao, S.J. et al., "The Interference of Ascorbate and Urca in Low–Potential Electrochemical Glucose Sensing". *Proceedings of the Twelfth Annual International Conference of the IEEE Engineering in Medicine and Biology Society*, 12(2): 487–489 (Nov. 1–4, 1990).
Yao, T. et al., "A Chronically–Modified Enzyme Membrane Electrode As An Amperometric Glucose Sensor," *Analytical Chimica Acta*, 148:27–33 (1983).
Ye, L. et al., "High Current Density "Wired"Ouinoprotein Glucose Dehydrogenase Electrode." *Anal. Chem.*65(3): 2389241 (Feb. 1, 1993).
Yildiz, A. et al., "Evlauation of an Improved Thin–Layer Electrode," *Analytical Chemistry*, 40(70): 1018–1024 (June 1968).
Zamzow, K. et al., New Wearable Continuous Blood Glucose Monitor (BGM) and Artificial Pancreas (AP), *Diabetes*. 39:5A(20)(May 1990).
Zhang, Y. et al., "Application of cell culture toxicity tests to the development of implantable biosensors," *Biosensors & Bioelectronics*, 6:653–661 (1991).
Zhang, Y. et al., "Elimination of ther Acetaminophen Interference in an Implantable Glucose Sensor," *Anal. Chem.*66:1183–1188 (1994).

* cited by examiner

# EXHIBIT 8

US006565509B1

(12) **United States Patent**
**Say et al.**

(10) **Patent No.: US 6,565,509 B1**
(45) **Date of Patent: May 20, 2003**

(54) **ANALYTE MONITORING DEVICE AND METHODS OF USE**

(75) Inventors: **James Say**, Alameda, CA (US); **Michael F. Tomasco**, Cupertino, CA (US); **Adam Heller**, Austin, TX (US); **Yoram Gal**, Kibbutz Yagur (IL); **Behrad Aria**, Alameda, CA (US); **Ephraim Heller**, Oakland, CA (US); **Phillip John Plante**, Sunnyvale, CA (US); **Mark S. Vreeke**, Alameda, CA (US); **Keith A. Friedman**, Austin, TX (US); **Fredric C. Colman**, Berkeley, CA (US)

(73) Assignee: **TheraSense, Inc.**, Alameda, CA (US)

( * ) Notice: Subject to any disclaimer, the term of this patent is extended or adjusted under 35 U.S.C. 154(b) by 104 days.

(21) Appl. No.: **09/667,199**

(22) Filed: **Sep. 21, 2000**

**Related U.S. Application Data**

(63) Continuation of application No. 09/070,677, filed on Apr. 30, 1998.

(51) **Int. Cl.**[7] ..... **A61B 5/00**; A61B 5/05

(52) **U.S. Cl.** ..... **600/365**; 600/347; 600/345

(58) **Field of Search** ..... 600/365, 345, 600/346, 347, 354, 357, 366, 309

(56) **References Cited**

U.S. PATENT DOCUMENTS

| | | | |
|---|---|---|---|
| 3,260,656 | A | 7/1966 | Ross, Jr. |
| 3,653,841 | A | 4/1972 | Klein |
| 3,719,564 | A | 3/1973 | Lilly, Jr. et al. |
| 3,776,832 | A | 12/1973 | Oswin et al. |
| 3,837,339 | A | 9/1974 | Aisenberg et al. |
| 3,926,760 | A | 12/1975 | Allen et al. |
| 3,972,320 | A | 8/1976 | Kalman |
| 3,979,274 | A | 9/1976 | Newman |
| 4,008,717 | A | 2/1977 | Kowarski |
| 4,016,866 | A | 4/1977 | Lawton |

(List continued on next page.)

FOREIGN PATENT DOCUMENTS

| | | |
|---|---|---|
| DE | 29 03 216 | 8/1979 |
| DE | 227 029 A3 | 9/1985 |

(List continued on next page.)

OTHER PUBLICATIONS

Abruña, H. D. et al., "Rectifying Interfaces Using Two–Layer Films of Electrochemically Polymerized Vinylpyridine and Vinylbipyridine Complexes of Ruthenium and Iron on Electrodes," *J. Am. Chem. Soc.*, 103(1):1–5 (Jan. 14, 1981).

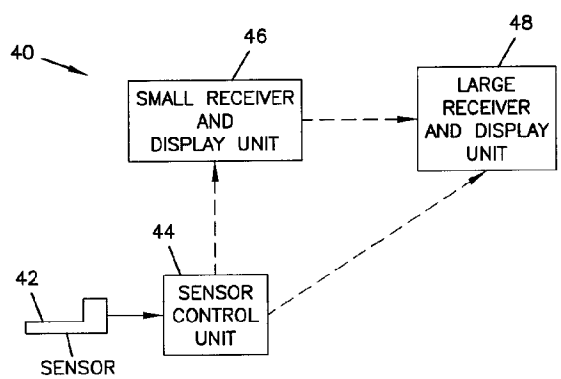
(List continued on next page.)

*Primary Examiner*—Max F. Hindenburg
*Assistant Examiner*—Navin Natnithithadha
(74) *Attorney, Agent, or Firm*—Merchant & Gould P.C.

(57) **ABSTRACT**

An analyte monitor includes a sensor, a sensor control unit, and a display unit. The sensor has, for example, a substrate, a recessed channel formed in the substrate, and conductive material disposed in the recessed channel to form a working electrode. The sensor control unit typically has a housing adapted for placement on skin and is adapted to receive a portion of an electrochemical sensor. The sensor control unit also includes two or more conductive contacts disposed on the housing and configured for coupling to two or more contact pads on the sensor. A transmitter is disposed in the housing and coupled to the plurality of conductive contacts for transmitting data obtained using the sensor. The display unit has a receiver for receiving data transmitted by the transmitter of the sensor control unit and a display coupled to the receiver for displaying an indication of a level of an analyte. The analyte monitor may also be part of a drug delivery system to alter the level of the analyte based on the data obtained using the sensor.

**56 Claims, 26 Drawing Sheets**



U.S. PATENT DOCUMENTS


| | | | |
|---|---|---|---|
| 4,055,175 | A | 10/1977 | Clemens et al. |
| 4,059,406 | A | 11/1977 | Fleet |
| 4,076,596 | A | 2/1978 | Connery et al. |
| 4,098,574 | A | 7/1978 | Dappen |
| 4,100,048 | A | 7/1978 | Pompei et al. |
| 4,151,845 | A | 5/1979 | Clemens |
| 4,168,205 | A | 9/1979 | Danninger et al. |
| 4,172,770 | A | 10/1979 | Semersky et al. |
| 4,178,916 | A | 12/1979 | McNamara |
| 4,206,755 | A | 6/1980 | Klein |
| 4,224,125 | A | 9/1980 | Nakamura et al. |
| 4,240,438 | A | 12/1980 | Updike et al. |
| 4,247,297 | A | 1/1981 | Berti et al. |
| 4,340,458 | A | 7/1982 | Lerner et al. |
| 4,352,960 | A | 10/1982 | Dormer et al. |
| 4,356,074 | A | 10/1982 | Johnson |
| 4,365,637 | A | 12/1982 | Johnson |
| 4,366,033 | A | 12/1982 | Richter et al. |
| 4,375,399 | A | 3/1983 | Havas et al. |
| 4,384,586 | A | 5/1983 | Christiansen |
| 4,390,621 | A | 6/1983 | Bauer |
| 4,401,122 | A | 8/1983 | Clark, Jr. |
| 4,404,066 | A | 9/1983 | Johnson |
| 4,418,148 | A | 11/1983 | Oberhardt |
| 4,427,770 | A | 1/1984 | Chen et al. |
| 4,431,004 | A | 2/1984 | Bessman et al. |
| 4,436,094 | A | 3/1984 | Cerami |
| 4,440,175 | A | 4/1984 | Wilkins |
| 4,450,842 | A | 5/1984 | Zick et al. |
| 4,458,686 | A | 7/1984 | Clark, Jr. |
| 4,461,691 | A | 7/1984 | Frank |
| 4,469,110 | A | 9/1984 | Slama |
| 4,477,314 | A | 10/1984 | Richter et al. |
| 4,484,987 | A | 11/1984 | Gough |
| 4,522,690 | A | 6/1985 | Venkatasetty |
| 4,524,114 | A | 6/1985 | Samuels et al. |
| 4,526,661 | A | 7/1985 | Steckhan et al. |
| 4,534,356 | A | 8/1985 | Papadakis |
| 4,538,616 | A | 9/1985 | Rogoff |
| 4,543,955 | A | 10/1985 | Schroeppel |
| 4,545,382 | A | 10/1985 | Higgins et al. |
| 4,552,840 | A | 11/1985 | Riffer |
| 4,560,534 | A | 12/1985 | Kung et al. |
| 4,571,292 | A | 2/1986 | Liu et al. |
| 4,573,994 | A | 3/1986 | Fischell et al. |
| 4,581,336 | A | 4/1986 | Malloy et al. |
| 4,595,011 | A | 6/1986 | Phillips |
| 4,619,754 | A | 10/1986 | Niki et al. |
| 4,627,445 | A | 12/1986 | Garcia et al. |
| 4,627,908 | A | 12/1986 | Miller |
| 4,633,878 | A | 1/1987 | Bombardieri |
| 4,637,403 | A | 1/1987 | Garcia et al. |
| 4,650,547 | A | 3/1987 | Gough |
| 4,654,197 | A | 3/1987 | Lilja et al. |
| 4,655,880 | A | 4/1987 | Liu |
| 4,655,885 | A | 4/1987 | Hill et al. |
| 4,671,288 | A | 6/1987 | Gough |
| 4,679,562 | A | 7/1987 | Luksha |
| 4,680,268 | A | 7/1987 | Clark, Jr. |
| 4,682,602 | A | 7/1987 | Prohaska |
| 4,684,537 | A | 8/1987 | Graetzel et al. |
| 4,685,463 | A | 8/1987 | Williams |
| 4,703,756 | A | 11/1987 | Gough et al. |
| 4,711,245 | A | 12/1987 | Higgins et al. |
| 4,717,673 | A | 1/1988 | Wrighton et al. |
| 4,721,601 | A | 1/1988 | Wrighton et al. |
| 4,721,677 | A | 1/1988 | Clark, Jr. |
| 4,726,378 | A | 2/1988 | Kaplan |
| 4,726,716 | A | 2/1988 | McGuire |
| 4,731,726 | A | 3/1988 | Allen, III |
| 4,757,022 | A | 7/1988 | Shults et al. |
| 4,758,323 | A | 7/1988 | Davis et al. |
| 4,759,371 | A | 7/1988 | Franetzki |
| 4,759,828 | A | 7/1988 | Young et al. |
| 4,764,416 | A | 8/1988 | Ueyama et al. |
| 4,776,944 | A | 10/1988 | Janata et al. |
| 4,781,798 | A | 11/1988 | Gough |
| 4,784,736 | A | 11/1988 | Lonsdale et al. |
| 4,795,707 | A | 1/1989 | Niiyama et al. |
| 4,796,634 | A | 1/1989 | Huntsman et al. |
| 4,805,624 | A | 2/1989 | Yao et al. |
| 4,813,424 | A | 3/1989 | Wilkins |
| 4,815,469 | A | 3/1989 | Cohen et al. |
| 4,820,399 | A | 4/1989 | Senda et al. |
| 4,822,337 | A | 4/1989 | Newhouse et al. |
| 4,830,959 | A | 5/1989 | McNeil et al. |
| 4,832,797 | A | 5/1989 | Vadgama et al. |
| RE32,947 | E | 6/1989 | Dormer et al. |
| 4,840,893 | A | 6/1989 | Hill et al. |
| 4,848,351 | A | 7/1989 | Finch |
| 4,871,351 | A | 10/1989 | Feingold |
| 4,871,440 | A | 10/1989 | Nagata et al. |
| 4,874,500 | A | 10/1989 | Madou et al. |
| 4,890,620 | A | 1/1990 | Gough |
| 4,894,137 | A | 1/1990 | Takizawa et al. |
| 4,897,162 | A | 1/1990 | Lewandowski et al. |
| 4,897,173 | A | 1/1990 | Nankai et al. |
| 4,909,908 | A | 3/1990 | Ross et al. |
| 4,911,794 | A | 3/1990 | Parce et al. |
| 4,917,800 | A | 4/1990 | Lonsdale et al. |
| 4,919,141 | A | 4/1990 | Zier et al. |
| 4,919,767 | A | 4/1990 | Vadgama et al. |
| 4,923,586 | A | 5/1990 | Katayama et al. |
| 4,927,516 | A | 5/1990 | Yamaguchi et al. |
| 4,934,369 | A | 6/1990 | Maxwell |
| 4,935,105 | A | 6/1990 | Churchouse |
| 4,935,345 | A | 6/1990 | Guilbeau et al. |
| 4,938,860 | A | 7/1990 | Wogoman |
| 4,944,299 | A | 7/1990 | Silvian |
| 4,950,378 | A | 8/1990 | Nagata |
| 4,953,552 | A | 9/1990 | DeMarzo |
| 4,954,129 | A | 9/1990 | Giuliani et al. |
| 4,969,468 | A | 11/1990 | Byers et al. |
| 4,970,145 | A | 11/1990 | Bennetto et al. |
| 4,974,929 | A | 12/1990 | Curry |
| 4,986,271 | A | 1/1991 | Wilkins |
| 4,994,167 | A | 2/1991 | Shults et al. |
| 5,001,054 | A | 3/1991 | Wagner |
| 5,050,612 | A | 9/1991 | Matsumura |
| 5,058,592 | A | 10/1991 | Whisler |
| 5,070,535 | A | 12/1991 | Hochmair et al. |
| 5,082,550 | A | 1/1992 | Rishpon et al. |
| 5,082,786 | A | 1/1992 | Nakamoto |
| 5,089,112 | A | 2/1992 | Skotheim et al. |
| 5,095,904 | A | 3/1992 | Seligman et al. |
| 5,101,814 | A | 4/1992 | Palti |
| 5,108,564 | A | 4/1992 | Szuminsky et al. |
| 5,109,850 | A | 5/1992 | Blanco et al. |
| 5,120,420 | A | 6/1992 | Nankai et al. |
| 5,126,034 | A | 6/1992 | Carter et al. |
| 5,133,856 | A | 7/1992 | Yamaguchi et al. |
| 5,135,003 | A | 8/1992 | Souma |
| 5,141,868 | A | 8/1992 | Shanks et al. |
| 5,161,532 | A | 11/1992 | Joseph |
| 5,165,407 | A | 11/1992 | Wilson et al. |
| 5,174,291 | A | 12/1992 | Schoonen et al. |
| 5,190,041 | A | 3/1993 | Palti |
| 5,192,416 | A | 3/1993 | Wang et al. |
| 5,198,367 | A | 3/1993 | Aizawa et al. |
| 5,202,261 | A | 4/1993 | Musho et al. |
| 5,205,920 | A | 4/1993 | Oyama et al. |

| | | | | |
|---|---|---|---|---|
| 5,208,154 | A | | 5/1993 | Weaver et al. |
| 5,209,229 | A | | 5/1993 | Gilli |
| 5,217,595 | A | | 6/1993 | Smith et al. |
| 5,229,282 | A | | 7/1993 | Yoshioka et al. |
| 5,250,439 | A | | 10/1993 | Musho et al. |
| 5,262,035 | A | | 11/1993 | Gregg et al. |
| 5,262,305 | A | | 11/1993 | Heller et al. |
| 5,264,103 | A | | 11/1993 | Yoshioka et al. |
| 5,264,104 | A | | 11/1993 | Gregg et al. |
| 5,264,106 | A | | 11/1993 | McAleer et al. |
| 5,271,815 | A | | 12/1993 | Wong |
| 5,279,294 | A | | 1/1994 | Anderson et al. |
| 5,286,362 | A | | 2/1994 | Hoenes et al. |
| 5,286,364 | A | | 2/1994 | Yacynych et al. |
| 5,288,636 | A | | 2/1994 | Pollmann et al. |
| 5,293,546 | A | | 3/1994 | Tadros et al. |
| 5,320,098 | A | | 6/1994 | Davidson |
| 5,320,725 | A | | 6/1994 | Gregg et al. |
| 5,322,063 | A | | 6/1994 | Allen et al. |
| 5,337,747 | A | | 8/1994 | Neftel |
| 5,352,348 | A | | 10/1994 | Young et al. |
| 5,356,786 | A | | 10/1994 | Heller et al. |
| 5,368,028 | A | | 11/1994 | Palti |
| 5,372,133 | A | | 12/1994 | Hogen Esch |
| 5,376,251 | A | | 12/1994 | Kaneko et al. |
| 5,378,628 | A | | 1/1995 | Grätzel et al. |
| 5,387,327 | A | | 2/1995 | Khan |
| 5,390,671 | A | | 2/1995 | Lord et al. |
| 5,391,250 | A | | 2/1995 | Cheney, II et al. |
| 5,395,504 | A | | 3/1995 | Saurer et al. |
| 5,400,782 | A | | 3/1995 | Beaubiah |
| 5,411,647 | A | | 5/1995 | Johnson et al. |
| 5,437,999 | A | | 8/1995 | Diebold et al. |
| 5,469,846 | A | | 11/1995 | Khan |
| 5,491,474 | A | | 2/1996 | Suni et al. |
| 5,494,562 | A | | 2/1996 | Maley et al. |
| 5,496,453 | A | | 3/1996 | Uenoyama et al. |
| 5,497,772 | A | | 3/1996 | Schulman et al. |
| 5,531,878 | A | | 7/1996 | Vadgama et al. |
| 5,545,191 | A | | 8/1996 | Mann et al. |
| 5,560,357 | A | | 10/1996 | Faupel et al. |
| 5,562,713 | A | | 10/1996 | Silvian |
| 5,565,085 | A | | 10/1996 | Ikeda et al. |
| 5,567,302 | A | | 10/1996 | Song et al. |
| 5,568,806 | A | | 10/1996 | Cheney, II et al. |
| 5,569,186 | A | | 10/1996 | Lord et al. |
| 5,582,184 | A | | 12/1996 | Erickson et al. |
| 5,582,697 | A | | 12/1996 | Ikeda et al. |
| 5,582,698 | A | | 12/1996 | Flaherty et al. |
| 5,586,553 | A | | 12/1996 | Halili et al. |
| 5,589,326 | A | | 12/1996 | Deng et al. |
| 5,593,852 | A | | 1/1997 | Heller et al. |
| 5,596,150 | A | | 1/1997 | Arndt et al. |
| 5,617,851 | A | | 4/1997 | Lipkovker |
| 5,628,890 | A | | 5/1997 | Carter et al. |
| 5,651,869 | A | | 7/1997 | Yoshioka et al. |
| 5,660,163 | A | | 8/1997 | Schulman et al. |
| 5,670,031 | A | | 9/1997 | Hintsche et al. |
| 5,680,858 | A | | 10/1997 | Hansen et al. |
| 5,682,233 | A | | 10/1997 | Brinda |
| 5,695,623 | A | | 12/1997 | Michel et al. |
| 5,708,247 | A | | 1/1998 | McAleer et al. |
| 5,711,001 | A | | 1/1998 | Iliff et al. |
| 5,711,861 | A | * | 1/1998 | Ward et al. ..... 204/403.09 |
| 5,711,862 | A | | 1/1998 | Sakoda et al. |
| 5,741,211 | A | | 4/1998 | Renirie et al. |
| 5,771,001 | A | | 6/1998 | Cobb |
| 5,791,344 | A | | 8/1998 | Schulman et al. |
| 5,800,420 | A | | 9/1998 | Gross et al. |
| 5,807,375 | A | | 9/1998 | Gross et al. |
| 5,820,551 | A | | 10/1998 | Hill et al. |
| 5,820,622 | A | | 10/1998 | Gross et al. |
| 5,822,715 | A | | 10/1998 | Worthington et al. |
| 5,827,184 | A | | 10/1998 | Netherly et al. |
| 5,840,020 | A | | 11/1998 | Heinonen et al. |
| 5,842,983 | A | | 12/1998 | Abel et al. |
| 5,885,211 | A | | 3/1999 | Eppstein et al. |
| 5,899,855 | A | | 5/1999 | Brown |
| 5,954,685 | A | | 9/1999 | Tierney |
| 5,971,922 | A | | 10/1999 | Arita et al. |
| 6,001,067 | A | * | 12/1999 | Shults et al. ..... 600/345 |
| 6,024,699 | A | | 2/2000 | Surwit et al. |
| 6,122,351 | A | | 9/2000 | Schlueter, Jr. et al. |

FOREIGN PATENT DOCUMENTS

| | | | |
|---|---|---|---|
| DE | 3934299 | | 10/1990 |
| EP | 0 010 375 | A1 | 4/1980 |
| EP | 0 026 995 | A1 | 4/1981 |
| EP | 0 048 090 | A2 | 3/1982 |
| EP | 0 078 636 | A1 | 5/1983 |
| EP | 0 096 288 | A1 | 12/1983 |
| EP | 0 125 139 | A2 | 11/1984 |
| EP | 0 127 958 | A2 | 12/1984 |
| EP | 0 136 362 | A1 | 4/1985 |
| EP | 0 170 375 | A2 | 2/1986 |
| EP | 0 177 743 | A2 | 4/1986 |
| EP | 0 080 304 | B1 | 5/1986 |
| EP | 0 184 909 | A2 | 6/1986 |
| EP | 0 206 218 | A2 | 12/1986 |
| EP | 0 230 472 | A1 | 8/1987 |
| EP | 0 241 309 | A3 | 10/1987 |
| EP | 0 245 073 | A2 | 11/1987 |
| EP | 0 278 647 | A2 | 8/1988 |
| EP | 0 359 831 | A1 | 3/1990 |
| EP | 0 368 209 | A1 | 5/1990 |
| EP | 0 390 390 | A1 | 10/1990 |
| EP | 0 400 918 | A1 | 12/1990 |
| EP | 0 453 283 | A1 | 10/1991 |
| EP | 0 470 290 | A1 | 2/1992 |
| EP | 0 127 958 | B2 | 3/1992 |
| EP | 0 255 291 | B1 | 6/1992 |
| GB | 1394171 | | 5/1975 |
| GB | 1599241 | A | 9/1981 |
| GB | 2 073 891 | A | 10/1981 |
| GB | 2 154 003 | B | 2/1988 |
| GB | 2 204 408 | A | 11/1988 |
| GB | 2 254 436 | A | 10/1992 |
| JP | 54-41191 | | 4/1979 |
| JP | 55-10581 | | 1/1980 |
| JP | 55-10583 | | 1/1980 |
| JP | 55-10584 | | 1/1980 |
| JP | 55-12406 | | 1/1980 |
| JP | 56-163447 | | 12/1981 |
| JP | 57-70448 | | 4/1982 |
| JP | 60-173457 | | 9/1985 |
| JP | 60-173458 | | 9/1985 |
| JP | 60-173459 | | 9/1985 |
| JP | 61-90050 | | 5/1986 |
| JP | 62-85855 | | 4/1987 |
| JP | 62-114747 | | 5/1987 |
| JP | 63-58149 | | 3/1988 |
| JP | 63-128252 | | 5/1988 |
| JP | 63-139246 | | 6/1988 |
| JP | 63-294799 | | 12/1988 |
| JP | 63-317757 | | 12/1988 |
| JP | 63-317758 | | 12/1988 |
| JP | 1-114746 | | 5/1989 |
| JP | 1-114747 | | 5/1989 |
| JP | 1-124060 | | 5/1989 |
| JP | 1-134244 | | 5/1989 |
| JP | 1-156658 | | 6/1989 |
| JP | 2-62958 | | 3/1990 |

| | | |
|---|---|---|
| JP | 2-120655 | 5/1990 |
| JP | 2-287145 | 11/1990 |
| JP | 2-310457 | 12/1990 |
| JP | 3-26956 | 2/1991 |
| JP | 3-28752 | 2/1991 |
| JP | 3-202764 | 9/1991 |
| JP | 5-72171 | 3/1993 |
| JP | 5-196595 | 8/1993 |
| JP | 5-190050 | 7/1994 |
| JP | 7-55757 A | 3/1995 |
| JP | 7-72585 | 3/1995 |
| JP | 8-285814 A | 11/1996 |
| JP | 8-285815 A | 11/1996 |
| JP | 9-21778 A | 1/1997 |
| JP | 9-101280 A | 4/1997 |
| JP | 9-285459 A | 11/1997 |
| JP | 10-170471 A | 6/1998 |
| SU | 1281988 A1 | 1/1987 |
| WO | WO 85/05119 | 11/1985 |
| WO | WO 89/08713 | 9/1989 |
| WO | WO 90/05300 | 5/1990 |
| WO | WO 90/05910 | 5/1990 |
| WO | WO 91/01680 | 2/1991 |
| WO | WO 91/04704 | 4/1991 |
| WO | WO 91/15993 | 10/1991 |
| WO | WO 92/13271 | 8/1992 |
| WO | WO 94/20602 | 9/1994 |
| WO | WO 94/27140 | 11/1994 |
| WO | WO 96/30431 | 10/1996 |
| WO | WO 97/02847 | 1/1997 |
| WO | WO 97/19344 | 5/1997 |
| WO | WO 97/42882 | 11/1997 |
| WO | WO 97/42883 | 11/1997 |
| WO | WO 97/42886 | 11/1997 |
| WO | WO 97/42888 | 11/1997 |
| WO | WO 97/43962 | 11/1997 |

## OTHER PUBLICATIONS

Albery, W. J. et al., "Amperometric enzyme electrodes. Part II. Conducting salts as electrode materials for the oxidation of glucose oxidase," *J. Electroanal. Chem. Interfacial Electrochem.,* 194(2) (1 page—Abstract only) (1985).

Albery, W. J. et al., "Amperometric Enzyme Electrodes," *Phil. Trans. R. Soc. Lond.* B316:107–119 (1987).

Alcock, S. J. et al., "Continuous Analyte Monitoring to Aid Clinical Practice," *IEEE Engineering in Medicine and Biology,* 319–325 (1994).

Anderson, L. B. et al., "Thin–Layer Electrochemistry: Steady–State Methods of Studying Rate Processes," *J. Electroanal. Chem.,* 10:295–395 (1965).

Bartlett, P. N. et al., "Covalent Binding of Electron Relays to Glucose Oxidation," *J. Chem. Soc. Chem. Commun.,* 1603–1604 (1987).

Bartlett, P. N. et al., "Modification of glucose oxidase by tetrathiafulvalene," *J. Chem. Soc., Chem. Commun.,* 16 (1 page—Abstract only) (1990).

Bartlett, P. N. et al., "Strategies for the Development of Amperometric Enzyme Electrodes," *Biosensors,* 3:359–379 (1987/88).

Bindra, D.S. et al., "Design and in Vitro Studies of a Needle–Type Glucose Sensor for Subcutaneous Monitoring", *Anal. Chem.,* 63(17):1692–1696 (Sep. 1, 1991).

Bobbioni–Harsch, E. et al., "Lifespan of subcutaneous glucose sensors and their performances during dynamic glycaemia changes in rats," *J. Biomed. Eng.* 15:457–463 (1993).

Brandt, J. et al., "Covalent attachment of proteins to polysaccharide carriers by means of benzoquinone," *Biochim. Biophys. Acta,* 386(1) (1 page Abstract only) (1975).

Brownlee, M. et al., "A Glucose–Controlled Insulin–Delivery System: Semisynthetic Insulin Bound to Lectin", *Science,* 206(4423):1190–1191 (Dec. 7, 1979).

Cass, A.E.G. et al., "Ferricinum Ion As An Electron Acceptor for Oxido–Reductases," *J. Electroanal. Chem.,* 190:117–127 (1985).

Cass, A.E.G. et al., "Ferrocene–Mediated Enzyme Electrode for Amperometric Determination of Glucose", *Anal. Chem.,* 56(4):667–671 (Apr. 1984).

Castner, J. F. et al., "Mass Transport and Reaction Kinetic Parameters Determined Electrochemically for Immobilized Glucose Oxidase," *Biochemistry,* 23(10):2203–2210 (1984).

Claremont, D.J. et al., "Biosensors for Continuous In Vivo Glucose Monitoring", *IEEE Engineering in Medicine and Biology Society 10th Annual International Conference,* New Orleans, Louisiana, 3 pgs. (Nov. 4–7, 1988).

Clark, L.C. et al., "Differential Anodic Enzyme Polarography for the Measurement of Glucose", *Oxygen Transport to Tissue: Instrumentation, Methods, and Physiology,* 127–132 (1973).

Clark, L.C., Jr. et al., "Electrode Systems for Continuous Monitoring in Cardiovascular Surgery," *Annals New York Academy of Sciences,* pp. 29–45 (1962).

Clark, L.C. et al., "Long–term Stability of Electroenzymatic Glucose Sensors Implanted in Mice," *Trans. Am. Soc. Artif. Intern. Organs,* XXXIV:259–265 (1988).

Clarke, W. L., et al., "Evaluating Clinical Accuracy of Systems for Self–Monitoring of Blood Glucose," *Diabetes Care,* 10(5):622–628 (Sep.–Oct. 1987).

Csöregi, E. et al., "Design, Characterization, and One–Point in Vivo Calibration of a Subcutaneously Implanted Glucose Electrode," *Anal. Chem.* 66(19):3131–3138 (Oct. 1, 1994).

Csöregi, E. et al., "Design and Optimization of a Selective Subcutaneously Implantable Glucose Electrode Based on "Wired" Glucose Oxidase," *Anal. Chem.* 67(7):1240–1244 (Apr. 1, 1995).

Csöregi, E. et al., "On–Line Glucose Monitoring by Using Microdialysis Sampling and Amperometric Detection Based on "Wired" Glucose Oxidase in Carbon Paste," *Mikrochim. Acta.* 121:31–40 (1995).

Davis, G., "Electrochemical Techniques for the Development of Amperometric Biosensors", *Biosensors,* 1:161–178 (1985).

Degani, Y. et al., "Direct Electrical Communication between Chemically Modified Enzymes and Metal Electrodes. 1. Electron Transfer from Glucose Oxidase to Metal Electrodes via Electron Relays, Bound Covalently to the Enzyme," *J. Phys. Chem.,* 91(6):1285–1289 (1987).

Degani, Y. et al., "Direct Electrical Communication between Chemically Modified Enzymes and Metal Electrodes. 2. Methods for Bonding Electron–Transfer Relays to Glucose Oxidase and D–Amino–Acid Oxidase," *J. Am. Chem. Soc.,* 110(8):2615–2620 (1988).

Degani, Y. et al., "Electrical Communication between Redox Centers of Glucose Oxidase and Electrodes via Electrostatically and Covalently Bound Redox Polymers," *J. Am. Chem. Soc.,* 111:2357–2358 (1989).

Denisevich, P. et al., "Unidirectional Current Flow and Charge State Trapping at Redox Polymer Interfaces on Bilayer Electrodes: Principles, Experimental Demonstration, and Theory," *J. Am. Chem. Soc.,* 103(16):4727–4737 (1981).

Dicks, J. M., "Ferrocene modified polypyrrole with immobilised glucose oxidase and its application in amperometric glucose microbiosensors," *Ann. Biol. clin.,* 47:607–619 (1989).

Engstrom, R.C., "Electrochemical Pretreatment of Glassy Carbon Electrodes", *Anal. Chem.,* 54(13):2310–2314 (Nov. 1982).

Engstrom, R.C. et al., "Characterization of Electrochemically Pretreated Glassy Carbon Electrodes", *Anal. Chem.,* 56(2):136–141 (Feb. 1984).

Ellis, C. D., "Selectivity and Directed Charge Transfer through an Electroactive Metallopolymer Film," *J. Am. Chem. Soc.,* 103(25):7480–7483 (1981).

Feldman, B.J. et al., "Electron Transfer Kinetics at Redox Polymer/Solution Interfaces Using Microelectrodes and Twin Electrode Thin Layer Cells", *J. Electroanal. Chem.,* 194(1):63–81 (Oct. 10, 1985).

Fischer, H. et al., "Intramolecular Electron Transfer Mediated by 4,4'–Bipyridine and Related Bridging Groups", *J. Am. Chem. Soc.,* 98(18):5512–5517 (Sep. 1, 1976).

Foulds, N.C. et al., "Enzyme Entrapment in Electrically Conducting Polymers," *J. Chem. Soc., Faraday Trans 1.,* 82:1259–1264 (1986).

Foulds, N.C. et al., "Immobilization of Glucose Oxidase in Ferrocene–Modified Pyrrole Polymers," *Anal. Chem.,* 60(22):2473–2478 (Nov. 15, 1988).

Frew, J.E. et al., "Electron–Transfer Biosensors", *Phil. Trans. R. Soc. Lond.,* B316:95–106 (1987).

Gorton, L. et al., "Selective detection in flow analysis based on the combination of immobilized enzymes and chemically modified electrodes," *Analytica Chimica Acta.,* 250:203–248 (1991).

Gregg, B. A. et al., "Cross–Linked Redox Gels Containing Glucose Oxidase for Amperometric Biosensor Applications," *Analytical Chemistry,* 62(3):258–263 (Feb. 1, 1990).

Gregg, B. A. et al., "Redox Polymer Films Containing Enzymes. 1. A Redox–Conducting Epoxy Cement: Synthesis, Characterization, and Electrocatalytic Oxidation of Hydroquinone," *J. Phys. Chem.,* 95(15):5970–5975 (1991).

Hale, P.D. et al., "A New Class of Amperometric Biosensor Incorporating a Polymeric Electron–Transfer Mediator," *J. Am. Chem. Soc.,* 111(9):3482–3484 (1989).

Harrison, D.J. et al., "Characterization of Perfluorosulfonic Acid Polymer Coated Enzyme Electrodes and a Miniaturized Integrated Potentiostat for Glucose Analysis in Whole Blood", *Anal. Chem.,* 60(19):2002–2007 (Oct. 1, 1988).

Hawkridge, F. M. et al., "Indirect Coulometric Titration of Biological Electron Transport Components," *Analytical Chemistry,* 45(7):1021–1027 (Jun. 1973).

Heller, A., "Amperometric biosensors based on three–dimensional hydrogel–forming epoxy networks," *Sensors and Actuators B,* 13–14:180–183 (1993).

Heller, A., "Electrical Connection of Enzyme Redox Centers to Electrodes," *J. Phys. Chem.,* 96(9):3579–3587 (1992).

Heller, A., "Electrical Wiring of Redox Enzymes," *Acc. Chem. Res.,* 23(5):129–134 (1990).

Ianniello, R.M. et al. "Immobilized Enzyme Chemically Modified Electrode as an Amperometric Sensor", *Anal. Chem.,* 53(13):2090–2095 (Nov. 1981).

Ianniello, R.M. et al., "Differential Pulse Voltammetric Study of Direct Electron Transfer in Glucose Oxidase Chemically Modified Graphite Electrodes", *Anal. Chem.,* 54(7):1098–1101 (Jun. 1981).

Ikeda, T. et al., "Glucose oxidase–immobilized benzoquinone–carbon paste electrode as a glucose sensor," *Agric. Biol. Chem.,* 49(2) (1 page—Abstract only) (1985).

Ikeda, T. et al., "Kinetics of Outer–Sphere Electron Transfers Between Metal Complexes in Solutions and Polymeric Films on Modified Electrodes", *J. Am. Chem. Soc.,* 103(25):7422–7425 (Dec. 16, 1981).

Johnson, J. M. et al., "Potential–Dependent Enzymatic Activity in an Enzyme Thin–Layer Cell," *Anal. Chem.* 54:1377–1383 (1982).

Johnson, K. W. et al., "Reproducible Electrodeposition of Biomolecules for the Fabrication of Miniature Electroenzymatic Biosensors", *Sensors and Actuators B Chemical,* B5:85–89 (1991).

Jönsson, G. et al., "An Amperometric Glucose Sensor Made by Modification of a Graphite Electrode Surface With Immobilized Glucose Oxidase and Adsorbed Mediator", *Biosensors,* 1:355–368 (1985).

Josowicz, M. et al., "Electrochemical Pretreatment of Thin Film Platinum Electrodes", *J. Electrochem. Soc.,* 135(1):112–115 (Jan. 1988).

Katakis, I. et al., "Electrostatic Control of the Electron Transfer Enabling Binding of Recombinant Glucose Oxidase and Redox Polyelectrolytes," *J. Am. Chem. Soc.,* 116(8):3617–3618 (1994).

Katakis, I. et al., "L–α–Glycerophosphate and L–Lactate Electrodes Based on the Electrochemical "Wiring" of Oxidases," *Analytical Chemistry,* 64(9):1008–1013 (May 1, 1992).

Kenausis, G. et al., "'Wiring' of glucose oxidase and lactate oxidase within a hydrogel made with poly(vinyl pyridine) complexed with $[Os(4,4'\text{–dimethoxy–}2,2'\text{–bipyridine})_2 Cl]^{+/2+}$," *J. Chem. Soc., Faraday Trans.,* 92(20):4131–4136 (1996).

Koudelka, M. et al., "In–Vivo Behaviour of Hypodermically Implanted Microfabricated Glucose Sensors", *Biosensors & Bioelectronics,* 6(1):31–36 (1991).

Kulys, J. et al., "Mediatorless peroxidase electrode and preparation of bienzyme sensors," *Bioelectrochemisty and Bioenergetics,* 24:305–311 (1990).

Lager, W. et al., "Implantable Electrocatalytic Glucose Sensor," *Horm. Metab. Res.,* 26:526–530 (Nov. 1994).

Lindner, E. et al. "Flexible (Kapton–Based) Microsensor Arrays of High Stability for Cardiovascular Applications", *J. Chem. Soc.Faraday Trans.,* 89(2):361–367 (Jan. 21, 1993).

Maidan, R. et al., "Elimination of Electrooxidizable Interferant–Produced Currents in Amperometric Biosensors," *Analytical Chemistry,* 64(23):2889–2896 (Dec. 1, 1992).

Mastrototaro, J.J. et al., "An Electroenzymatic Glucose Sensor Fabricated on a Flexible Substrate", *Sensors and Biosensors B Chemical,* B5:139–144 (1991).

McNeil, C. J. et al., "Thermostable Reduced Nicotinamide Adenine Dinucleotide Oxidase: Application to Amperometric Enzyme Assay," *Anal. Chem.,* 61(1):25–29 (Jan. 1, 1989).

Miyawaki, O. et al., "Electrochemical and Glucose Oxidase Coenzyme Activity of Flavin Adenine Dinucleotide Covalently Attached to Glassy Carbon at the Adenine Amino Group", *Biochimica et Biophysica Acta,* 838:60–68 (1985).

Moatti–Sirat, D. et al., "Evaluating *in vitro* and *in vivo* the inteference of ascorbate and acetaminophen on glucose detection by a needle–type glucose sensor," *Biosensors & Bioelectronics,* 7(5):345–352 (1992).

Moatti–Sirat, D. et al., "Reduction of acetaminophen interference in glucose sensors by a composite Nafion membrane: demonstration in rats and man," *Diabetologia,* 37(6) (1 page—Abstract only) (Jun. 1994).

Moatti–Sirat, D. et al., "Towards continuous glucose monitoring: in vivo evaluation of a miniaturized glucose sensor implanted for several days in rat subcutaneous tissue," *Diabetologia,* 35(3) (1 page—Abstract only) (Mar. 1992).

Nagy, G. et al., "A New Type of Enzyme Electrode: The Ascorbic Acid Eliminator Electrode," *Life Sciences,* 31(23):2611–2616 (1982).

Nakamura, S. et al., "Effect of Periodate Oxidation on the Structure and Properties of Glucose Oxidase," *Biochimica et Biophysica Acta.,* 445:294–308 (1976).

Narazimhan, K. et al., "p–Benzoquinone activation of metal oxide electrodes for attachment of enzymes," *Enzyme Microb. Technol.,* 7(6) (1 page—Abstract only) (1985).

Ohara, T. J. et al., "Glucose Electrodes Based on Cross–Linked $[Os(bpy)_2CI]^{+/2+}$ Complexed Poly(1–vinylimadazole) Films," *Analytical Chemistry,* 65(23):3512–3516 (Dec. 1, 1993).

Ohara, T. J., "Osmium Bipyridyl Redox Polymers Used in Enzyme Electrodes," *Platinum Metals Rev.,* 39(2):54–62 (Apr. 1995).

Ohara, T. J. et al., ""Wired" Enzyme Electrodes for Amperometric Determination of Glucose or Lactate in the Presence of Interfering Substances," *Analytical Chemistry,* 66(15):2451–2457 (Aug. 1, 1994).

Olievier, C. N. et al., "In vivo Measurement of Carbon Dioxide Tension with a Miniature Electrode," *Pflugers Arch.* 373:269–272 (1978).

Paddock, R. et al., "Electrocatalytic reduction of hydrogen peroxide via direct electron transfer from pyrolytic graphite electrodes to irreversibly adsorbed cytochrome *c* peroxidase," *J. Electroanal. Chem.,* 260:487–494 (1989).

Palleschi, G. et al., "A Study of Interferences in Glucose Measurements in Blood by Hydrogen Peroxide Based Glucose Probes", *Anal. Biochem.,* 159:114–121 (1986).

Pankratov, I. et al., "Sol–gel derived renewable–surface biosensors," *Journal of Electroanalytical Chemistry,* 393:35–41 (1995).

Pathak, C. P. et al., "Rapid Photopolymerization of Immunoprotective Gels in Contact with Cells and Tissue," *J. Am. Chem. Soc.,* 114(21):8311–8312 (1992).

Pickup, J., "Developing glucose sensors for *in vivo* use," *Tibtech,* 11: 285–289 (Jul. 1993).

Pickup, J. C. et al., "In vivo molecular sensing in diabetes mellitus: an implantable glucose sensor with direct electron transfer," *Diabetologia,* 32(3):213–217 (1989).

Pickup, J. et al., "Potentially–implantable, amperometric glucose sensors with mediated electron transfer: improving the operating stability," *Biosensors,* 4(2) (1 page—Abstract only) (1989).

Pishko, M. V. et al., "Amperometric Glucose Microelectrodes Prepared Through Immobilization of Glucose Oxidase in Redox Hydrogels", *Anal. Chem.,* 63(20):2268–2272 (Oct. 15, 1991).

Poitout, V. et al., "A glucose monitoring system for on line estimation in man of blood glucose concentration using a miniaturized glucose sensor implanted in the subcutaneous tissue and a wearable control unit," *Diabetolgia,* 36(7) (1 page—Abstract only) (Jul. 1993).

Poitout, V. et al., "Calibration in dogs of a subcutaneous miniaturized glucose sensor using a glucose meter for blood glucose determination," *Biosensors & Bioelectronics,* 7:587–592 (1992).

Poitout, V. et al., "In vitro and in vivo evaluation in dogs of a miniaturized glucose sensor," *ASAIO Transactions,* 37(3) (1 page—Abstract only) (Jul.–Sep. 1991).

Pollak, A. et al., "Enzyme Immobilization by Condensation Copolymerization into Cross–Linked Polyacrylamide Gels," *J. Am. Chem. Soc.,* 102(20):6324–6336 (1980).

Reach, G. et al., "Can Continuous Glucose Monitoring Be Used for the Treatment of Diabetes?" *Analytical Chemistry,* 64(6):381–386 (Mar. 15, 1992).

Rebrin, K. et al., "Automated Feedback Control of Subcutaneous Glucose Concentration in Diabetic Dogs", *Diabetologia,* 32(8):573–576 (Aug. 1989).

Sakakida, M. et al., "Ferrocene–mediate needle–type glucose sensor covered with newly designed biocompatible membrane," *Sensors and Actuators B,* 13–14:319–322 (1993).

Samuels, G. J. et al., "An Electrode–Supported Oxidation Catalyst Based on Ruthenium (IV). pH "Encapsulation" in a Polymer Film," *J. Am. Chem. Soc.,* 103(2):307–312 (1981).

Sasso, S.V. et al., "Electropolymerized 1,2–Diaminobenzene as a Means to Prevent Interferences and Fouling and to Stabilize Immobilized Enzyme in Electrochemical Biosensors", *Anal. Chem.,* 62(11):1111–1117 (Jun. 1, 1990).

Scheller, F. et al., "Enzyme electrodes and their application," *Phil. Trans. R. Soc. Lond.,* B 316:85–94 (1987).

Schmehl, R.H. et al., "The Effect of Redox Site Concentration on the Rate of Mediated Oxidation of Solution Substrates by a Redox Copolymer Film", *J. Electroanal. Chem.,* 152:97–109 (Aug. 25, 1983).

Shichiri, M. et al., "Glycaemic Control in Pancreatetomized Dogs with a Wearable Artificial Endocrine Pancreas", *Diabetologia,* 24(3):179–184 (Mar. 1983).

Sittampalam, G. et al., "Surface–Modified Electrochemical Detector for Liquid Chromatography", *Anal. Chem.,* 55(9):1608–1610 (Aug. 1983).

Soegijoko, S. et al., *Horm. Metabl. Res., Suppl. Ser,* 12 (1 page—Abstract only) (1982).

Sprules, S. D. et al., "Evaluation of a New Disposable Screen–Printed Sensor Strip for the Measurement of NADH and Its Modification to Produce a Lactate Biosensor Employing Microliter Volumes," *Electroanalysis,* 8(6):539–543 (1996).

Sternberg, F. et al., "Calibration Problems of Subcutaneous Glucosensors when Applied "In–Situ" in Man," *Horm. metabl. Res,* 26:524–525 (1994).

Sternberg, R. et al., "Covalent Enzyme Coupling on Cellulose Acetate Membranes for Glucose Sensor Development," *Analytical Chemistry,* 60(24):2781–2786 (Dec. 15, 1998).

Sternberg, R. et al., "Study and Development of Multilayer Needle–type Enzyme–based Glucose Microsensors," *Biosensors,* 4:27–40 (1988).

Suekane, M., "Immobilization of glucose isomerase," *Zeitschrift für Allgemeine Mikrobiologie,* 22(8):565–576 (1982).

Tajima, S. et al., "Simultaneous Determination of Glucose and 1,5–Anydroglucitol", *Chemical Abstracts,* 111(25):394 111:228556g (Dec. 18, 1989).
Tarasevich, M.R. "Bioelectrocatalysis", *Comprehensive Treatise of Electrochemistry,* 10 (Ch. 4):231–295 (1985).
Tatsuma, T. et al., "Enzyme Monolayer– and Bilayer–Modified Tin Oxide Electrodes for the Determination of Hydrogen Peroxide and Glucose," *Anal. Chem.,* 61(21):2352–2355 (Nov. 1, 1989).
Taylor, C. et al., "'Wiring' of glucose oxidase within a hydrogel made with polyvinyl imidazole complexed with [(OS–4,4'–dimethoxy–2,2'–bipyridine)Cl]$^{+/2+}$," *Journal of Electroanalytical Chemistry,* 396:511–515 (1995).
Trojanowicz, M. et al., "Enzyme Entrapped Polypyrrole Modified Electrode for Flow–Injection Determination of Glucose," *Biosensors & Bioelectronics,* 5:149–156 (1990).
Turner, A.P.F. et al., "Diabetes Mellitus: Biosensors for Research and Management", *Biosensors,* 1:85–115 (1985).
Turner, R. F. B. et al., "A Biocompatible Enzyme Electrode for Continuous *in vivo* Glucose Monitoring in Whole Blood," *Sensors and Actuators,* B1(1–6):561–564 (Jan. 1990).
Tuzhi, P. et al., "Constant Potential Pretreatment of Carbon Fiber Electrodes for In Vivo Electrochemistry", *Analytical Letters,* 24(6):935–945 (1991).
Umaha, M., "Protein–Modified Electrochemically Active Biomaterial Surface," *U.S. Army Research Office Report,* (12 pages) (Dec. 1988).
Urban, G. et al., "Miniaturized Thin–Film Biosensors Using Covalently Immobilized Glucose Oxidase", *Biosensors & Bioelectronics,* 6(7):555–562 (1991).
Velho, G. et al., "In Vitro and In Vivo Stability of Electrode Potentials in Needle–Type Glucose Sensors", *Diabetes,* 38(2):164–171 (Feb. 1989).
Velho, G. et al., "Strategies for calibrating a subcutaneous glucose sensor", *Biomed. Biochin. Acta,* 48(11/12):957–964 (1989).
Von Woedtke, T. et al., "In Situ Calibration of Implanted Electrochemical Glucose Sensors," *Biomed. Biochim. Acta,* 48(11/12):943–952 (1989).
Vreeke, M. S. et al., "Chapter 15: Hydrogen Peroxide Electrodes Based on Electrical Connection of Redox Centers of Various Peroxidases to Electrodes through a Three–Dimensional Electron–Relaying Polymer Network," *Diagnostic Biosensor Polymers,* 7 pgs. (Jul. 26, 1993).
Vreeke, M. et al., "Hydrogen Peroxide and β–Nicotinamide Adenine Dinucleotide Sensing Amperometric Electrodes Based on Electrical Connection of Horseradish Peroxidase Redox Centers to Electrodes through a Three–Dimensional Electron Relaying Polymer Network," *Analytical Chemistry,* 64(24):3084–3090 (Dec. 15, 1992).
Wang, J. et al., "Activation of Glassy Carbon Electrodes by Alternating Current Electrochemical Treatment", *Analytica Chimica Acta,* 167:325–334 (Jan. 1985).
Wang, J. et al., "Amperometric biosensing of organic peroxides with peroxidase–modified electrodes," *Analytica Chimica Acta.* 254:81–88 (1991).
Wang, D. L. et al., "Miniaturized Flexible Amperometric Lactate Probe", *Analytical Chemistry,* 65(8):1069–1073 (Apr. 15, 1993).
Wang, J. et al., "Screen–Printable Sol–Gel Enzyme–Containing Carbon Inks," *Analytical Chemistry,* 68(15):2705–2708 (Aug. 1, 1996).
Wang, J. et al., "Sol–Gel–Derived Metal–Dispersed Carbon Composite Amperometric Biosensors," *Electroanalysis,* 9(1):52–55 (1997).
Williams, D.L. et al., "Electrochemical–Enzymatic Analysis of Blood Glucose and Lactate", *Anal. Chem.,* 42(1):118–121 (Jan. 1970).
Wilson, G. S. et al., "Progress toward the Development of an Implantable Sensor for Glucose," *Clinical Chemistry,* 38(9):1613–1617 (1992).
Yabuki, S. et al., "Electro–conductive Enzyme Membrane," *J. Chem. Soc. Chem. Commun,* 945–946 (1989).
Yang, L. et al., "Determination of Oxidase Enzyme Substrates Using Cross–Flow Thin–Layer Amperometry," *Electroanalysis,* 8(8–9):716–721 (1996).
Yao, S.J. et al., "The Interference of Ascorbate and Urea in Low–Potential Electrochemical Glucose Sensing", *Proceedings of the Twelfth Annual International Conference of the IEEE Engineering in Medicine and Biology Society,* 12(2):487–489 (Nov. 1–4, 1990).
Yao, T. et al., "A Chemically–Modified Enzyme Membrane Electrode As An Amperometric Glucose Sensor," *Analytica Chimica Acta.,* 148:27–33 (1983).
Ye, L. et al., "High Current Density "Wired " Quinoprotein Glucose Dehydrogenase Electrode," *Anal. Chem.,* 65(3):238–241 (Feb. 1, 1993).
Yildiz, A. et al., "Evaluation of an Improved Thin–Layer Electrode," *Analytical Chemistry,* 40(70):1018–1024 (Jun. 1968).
Zamzow, K. et al., New Wearable Continuous Blood Glucose Monitor (BGM) and Artificial Pancreas (AP), *Diabetes,* 39:5A(20) (May 1990).
Zhang, Y. et al., "Application of cell culture toxicity tests to the development of implantable biosensors," *Biosensors & Bioelectronics,* 6:653–661 (1991).
Zhang, Y. et al., "Elimination of the Acetaminophen Interference in an Implantable Glucose Sensor," *Anal. Chem.* 66:1183–1188 (1994).

* cited by examiner

# EXHIBIT 9

PATENT
Docket No. 518852800400

+CERTIFICATE OF MAILING BY "EXPRESS MAIL"

Express Mail Label No.: EV 761644564 US Date of Deposit: January 25, 2006

I hereby certify that this paper or fee is being deposited with the United States Postal Service "Express Mail Post Office to Addressee" service under 37 C.F.R. § 1.10 on the date indicated above and is addressed to: Mail Stop Ex Parte Reexam, Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.

Diane Blevins

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In the Reexamination of:

James SAY et al.

Patent No.: 6,565,509 B1

Issue Date: May 20, 2003

Issued To: TheraSense, Inc.

Examiner: To be assigned

**REQUEST FOR REEXAMINATION UNDER 37 C.F.R. § 1.510**

Mail Stop Ex Parte Reexam
Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Dear Sir:

On behalf of Dexcom, Inc. (hereafter "Requester"), the undersigned hereby submit under provisions of C.F.R. § 1.501 *et seq.*, a Request for Reexamination of claims 1-19, 24-26 and 35-38 of the above captioned U.S. Patent No. 6,565,509 to Say et al., entitled "ANALYTE MONITORING DEVICE AND METHODS OF USE," filed on September 21, 2000, and issued on May 20, 2003 (hereafter "the '509 patent"). The '509 patent was filed as a continuation of Application No. 09/070,677, filed April 30, 1998 (now U.S. 6,175,752). The '509 patent was

originally assigned to TheraSense, Inc. ("Patentee"). This Request for Reexamination is based upon the following prior art references:

(1) EP Patent Application No. 83106571.9 to Shichiri et al., entitled "Portable Artificial Pancreas," filed July 5, 1983, published January 18, 1984 as EP publication no. 0098592 A2, citable under 35 U.S.C. §§ 102(a) and (b), and attached hereto as Exhibit 1 (hereinafter "Shichiri I");

(2) Shichiri et al., "Telemetry Glucose Monitoring Device With Needle-Type Glucose Sensor: A Useful Tool for Blood Glucose Monitoring in Diabetic Individuals," Diabetes Care, Vol. 9, No. 3, pp. 298-301, May-June 1986, citable under 35 U.S.C. §§ 102(a) and (b), and attached hereto as Exhibit 2 (hereinafter "Shichiri II");

(3) Ko et al., (Ed.), "Implantable Sensors for Closed-Loop Prosthetic Systems," Mount Kisco, NY: Futura Publishing Company, Inc., 1985, Chapter 15, entitled "Needle-type Glucose Sensor for Wearable Artificial Endocrine Pancreas," pp. 197-210, citable under 35 U.S.C. §§ 102(a) and (b), and attached hereto as Exhibit 3 (Shichiri III),

(4) U.S. Patent No. 5,569,186 to Lord et al., entitled "Closed Loop Infusion Pump System With Removable Glucose Sensor," filed April 25, 1994, issued October 29, 1996, citable under 35 U.S.C. §§ 102(a), (b) and (e), and attached hereto as Exhibit 4 (hereinafter "Lord I");

(5) U.S. Patent No. 4,494,950 to Fischell, entitled "Plural Module Medication Delivery System," filed January 19, 1982 and issued January 22, 1985, citable under 35 U.S.C. §§ 102(a), (b) and (e), and attached hereto as Exhibit 5 (hereinafter "Fischell");

(6) M. Shichiri et al., "Glycaemic Control in Pancreatectomized Dogs with a Wearable Artificial Endocrine Pancreas," Diabetologia (1983) 24:179-184, Springer-Verlag 1983, citable under 35 U.S.C. §§ 102(a) and (b), and attached hereto as Exhibit 6 (hereinafter "Shichiri IV");

(7) U.S. Patent No. 5,390,671 to Lord et al., entitled "Transcutaneous Sensor Insertion Set," filed March 15, 1994, issued February 21, 1995, citable under 35 U.S.C. §§ 102(a), (b) and (e), and attached hereto as Exhibit 7 (hereinafter "Lord II");

(8) PCT Application No. PCT/US96/02006 to Cheney et al., entitled "Transcutaneous Sensor Insertion Set," filed February 14, 1996, claiming priority to U.S. application no. 08/393,159, published on August 22, 1996 as WO 96/25089, citable under 35 U.S.C. §§ 102(a) and (b), and attached hereto as Exhibit 8 (hereinafter "Cheney");

(9) U.S. Patent No. 5,957,854 to Besson et al., entitled "Wireless Medical Diagnosis And Monitoring Equipment," filed December 5, 1997, claiming priority to PCT/EP94/02926, filed September 2, 1994 (now U.S. 5,862,803), citable under 35 U.S.C. §§ 102(a) and (e), and attached hereto as Exhibit 9 (hereinafter "Besson");

(10) U.S. Patent No. 6,219,574 to Cormier et al., entitled "Device And Method For Enhancing Transdermal Sampling," filed June 17, 1997, claiming priority to provisional application no. 60/019,990, filed June 18, 1996, issued on April 17, 2001, citable under 35 U.S.C. § 102(e), and attached hereto as Exhibit 10 (hereinafter "Cormier");

(11) U.S. Patent No. 4,703,756 to Gough et al., entitled "Complete Glucose Monitoring System With An Implantable Telemetered Sensor Module," filed May 6, 1986, issued November 3, 1987, citable under 35 U.S.C. §§ 102(a), (b) and (e), and attached hereto as Exhibit 11 (hereinafter "Gough");

(12) Stuart J. Updike et al., "Principles of Long-term Fully Implanted Sensors With Emphasis On Radiotelemetric Monitoring of Blood Glucose From Inside a Subcutaneous Foreign Body Capsule (FBC)," Biosensors in the Body: Continuous in vivo Monitoring," Edited by David M. Fraser, Chapter 4, pp. 117-137, April 16, 1997. John Wiley & Sons Ltd, citable under 35 U.S.C. §§ 102(a) and (b) and attached hereto as Exhibit 12 (hereinafter "Updike");

(13) Mark C. Shults et al., "A Telemetry-Instrumentation System for Monitoring Multiple Subcutaneously Implanted Glucose Sensors," IEEE Transactions On Biomedical Engineering, Vol. 41, No. 10, pp. 937-942, October 1994. © 1994 IEEE, citable under 35 U.S.C. §§ 102(a) and (b), and attached hereto as Exhibit 13 (hereinafter "Shults");

(14) Brian D. McKean et al. "A Telemetry-Instrumentation System for Chronically Implanted Glucose and Oxygen Sensors," IEEE Transactions On Biomedical Engineering, Vol.

35, No. 7, © July 1988 IEEE, citable under 35 U.S.C. §§ 102(a) and (b), and attached hereto as Exhibit 14 (hereinafter "McKean");

(15) Jon C. Armour et al., "Application of Chronic Intravascular Blood Glucose Sensor in Dogs," Diabetes, Vol. 39, December 1990, citable under 35 U.S.C. §§ 102(a) and (b), and attached hereto as Exhibit 15 (hereinafter "Armour");

(16) Michael Thompson et al., "*In Vivo* Probes: Problems and Perspectives," Clinical Biochemistry, Vol. 19, October 1986, citable under 35 U.S.C. §§ 102(a) and (b), and attached hereto as Exhibit 16 (hereinafter "Thompson"); and

(17) G. Velho et al., "Strategies for calibrating a subcutaneous glucose sensor," Biomed. Biochim. Acta 48 (presented at the International Workshop on Intracorporeal Glucose Sensors," September 27-30, 1988, Göhren-Lebbin, GDR), citable under 35 U.S.C. §§ 102(a) and (b), and attached hereto as Exhibit 17 (hereinafter "Velho").

Pursuant to 35 U.S.C. § 303, Requester submits that the above-listed prior art references raise "substantial new questions of patentability" with respect to at least claims 1-19, 24-26 and 35-38 of the '509 patent. As required by 37 C.F.R. § 1.510(b)(1), a statement pointing out each substantial new question of patentability is provided below for each identified claim for which reexamination is requested. Furthermore, a detailed explanation of the pertinence and manner of applying the cited patents and publications to each identified claim is provided pursuant to 37 C.F.R. § 1.510(b)(2). As required by 37 C.F.R. §§ 1.510(b)(3) and 1.510(b)(4), copies of the pertinent patents and publications relied upon, and a copy of the entire '509 patent including the front face, drawings, specification and claims (in double column format) are included. The fee for requesting reexamination under 37 C.F.R. 1.20(c) is also enclosed.

## I. Introduction

### A. The '509 patent

Generally, the '509 patent is directed to an analyte monitoring device that includes a transcutaneous electrochemical sensor, a sensor control unit and a display unit configured to receive radio frequency (rf) signals from the sensor control unit. The sensor control unit has a

housing adapted for placement on a patient's skin and adapted to receive a portion of an electrochemical sensor. The sensor control unit also includes two or more conductive contacts disposed on the housing and configured for coupling to two or more contact pads on the electrochemical sensor. A transmitter is disposed in the housing of the sensor control unit and coupled to the plurality of conductive contacts for transmitting data obtained by the electrochemical sensor. As described in further detail below, however, prior art devices and systems taught each of the various embodiments of the purported invention recited in the identified claims of the '509 patent for which reexamination is requested. Because the prior art references disclose and teach each and every element of the identified claims, each of these claims are anticipated and/or rendered obvious by the prior art references.

It is noted that in the context of reexamining patent claims, "the PTO must apply the broadest reasonable meaning to the claim language, taking into account any definitions presented in the specification. *In re Bass*, 314 F.3d 575, 577 (Fed. Cir. 2002) (citing *In re Yamamoto*, 740 F.2d 1569, 1571 (Fed. Cir. 1984). Giving claims their broadest reasonable construction "serves the public interest by reducing the possibility that claims, finally allowed, will be given broader scope than is justified." *In re Yamamoto*, 740 F.2d at 1571. "Construing claims broadly during prosecution is not unfair to the applicant (or, in this case, the patentee), because the applicant has the opportunity to amend the claims to obtain more precise claim coverage." *In re American Academy of Science Tech Center*, 367 F.3d 1359, 1363 (Fed. Cir. 2004) (citing *Yamamoto*, 740 F.2d at 1571-72).

While the meaning of claims of issued patents are interpreted in light of the specification, prosecution history, prior art and other claims, this is not the mode of claim interpretation to be applied during examination. During examination, the claims must be interpreted as broadly as their terms reasonably allow. MPEP § 2111.01 (emphasis in original). "The USPTO uses a different standard for construing claims than that used by district courts; during examination the USPTO must give claims their broadest reasonable interpretations." *Id.* (citing *In re American Academy of Science Tech Center, supra*). This means that the words of the claim must be given

Additionally, during prosecution of the corresponding European patent application no. EP 1 075 209 (hereinafter "EP 209"), the patentee admitted that certain features of its claimed sensor control unit were known in the prior art. EP 209 is a National Phase application based on PCT application no. PCT/US99/01229 (attached hereto as Exhibit 19), which in turn claims priority to U.S. application no. 09/070,677, now U.S. 6,175,752 ("the '752 patent"). The present '509 patent at issue is a continuation of the '752 patent.

The claims of the EP 209 application were added to replace the claims originally filed in PCT application no. PCT/US99/01229, from which EP 209 was based. (See Exhibit 20, Cover letter and Chart comparing new claims to originally pending PCT claims).

During prosecution of the EP 209 application, the European Patent Office ("EPO") rejected the following claim 1 of EP 209 for lack of novelty over D1 (Lord I):

> 1. A sensor control unit comprising:
>
> a housing adapted for placement on skin and adapted to receive a portion of an electrochemical sensor extending out of the skin;
>
> at least one conductive contact configured for contacting at least one contact pad disposed on the portion of an electrochemical sensor extending out of the skin; and
>
> an rf transmitter disposed in the housing and coupled to the at least one conductive contact for transmitting data obtained using the electrochemical sensor.

(Exhibit 21, EPO December 20, 2004 Office Action at page 1).

The EPO further required the applicant to draft claims in two part form "with those features known in combination from the prior art being placed in the preamble . . . and with the remaining features being included in a characterising part" in accordance with Rule 29(1) EPC. (*Id.* at page 2).

In response to the EPO's prior art rejection, the EP 209 applicant amended claim 1 according to the EPO's two-part requirement as follows:

> 1. A sensor control unit (44, 254) comprising:

The above plain meaning of "transcutaneous" is also consistent with the specification of the '509 patent, which describes a transcutaneous sensor 42 having a distal end 67 that is subcutaneously implanted into the skin of a patient and a proximal end 65 which extends out of the skin of the patient to facilitate electrical connection between sensor electrodes 58 and 60 and corresponding contacts on a control unit 44. The sensor 42 is formed on a substrate 50 and sensor electrodes 58 and 60 are formed at the distal end 67 of the sensor 42 by conductive traces 52 applied or embedded in the substrate 50. The conductive traces 52 extend from the distal end 67 to the proximal end 65, where contact pads 49 on the substrate 50 provide electrical contact between the traces 52 and conductive contacts of the sensor control unit 44. (See, e.g., '509 patent, col. 9, lines 4-33, Figure 2; and col. 14, lines 14-27, Figure 1).

Thus, the '509 patent describes a transcutaneous sensor 42 having subcutaneously implanted electrodes 58 and 60 and conductive traces 52 formed on a substrate 50 that pass through and out of a patient's skin to provide electrical connection, via contact pads 49 formed on the substrate, between the electrodes 58 and 60 and conductive contacts of an external sensor control unit 44. Therefore, it is clear from the '509 patent that one or more transcutaneous electrical conductors (i.e., conductive traces 52), which provide electrical connection to the subcutaneously implanted electrodes 58 and 60, are part of the sensor 42.

The '509 patent defines "non-leachable" as "affixed on the sensor such that it does not substantially diffuse away from the working surface of the working electrode for the period in which the sensor is used (e.g., the period in which the sensor is implanted in a patient or measuring a sample)." (The '509 patent, at col. 5:66-6:5).

**b) Shichiri I discloses a transcutaneous electrochemical sensor having a nonleachable glucose sensing enzyme**

Shichiri I discloses an "electrode means 13 . . . adapted to measure blood glucose concentrations based on current resulting from electrolysis of hydrogen peroxide which is produced from *glucose in the presence of glucose oxidase serving as a catalyst.*" (p. 8, lines 19-23). Shichiri I further discloses that its "electrode means 13 comprises a platinum electrode

(anode) 34 and a silver electrode (cathode) 35 . . . with an *immobilized glucose oxidase membrane* 41" laminated to the outer surface of a hydrophilic semipermeable membrane 40, which in turn is laminated to the front end 36 of the platinum electrode 34. (p. 9, lines 1-18; Fig. 3).

"The platinum electrode 34 is inserted in a stainless steel cylinder 38 having the silver electrode 35 formed over its outer surface. . . . The platinum electrode 34 and the cylinder 38 are *connected, at there rear ends, to insulated lead wires 43 and 44*, respectively. The measuring electrode means 13 is attached to the forward end of a catheter 45 to be lodged in vivo and is inserted into the blood vessel or *beneath the skin*. The signal from the electrode means 13 is fed to the polarography electric circuit 14 through the catheter 45. (p. 9, lines 5 to p. 10, line 3; Fig. 3) (emphasis added).

Based on the foregoing description, it is clear that Shichiri I discloses a sensor assembly comprising a subcutaneously implantable electrode 13 connected to conductive lead wires 43 and 44, which extend transcutaneously out of the patient's skin to make electrical contact with external circuitry 14 configured to receive and process the signals from the electrode 13. As discussed above, the '509 patent makes it clear that an electric connection, *e.g.*, a conductive trace, is considered part of the sensor. Accordingly, the conductive lead wires 43 and 44 are part of the sensor disclosed in Shichiri I.

The '509 patent defines non-leachable as follows:

> A "non-leachable" or "non-releasable" compound or a compound that is "non-leachably disposed" is meant to define a compound that is affixed on the sensor such that it does not substantially diffuse away from the working surface of the working electrode for the period in which the sensor is used (e.g., the period in which the sensor is implanted in a patient or measuring a sample).

(The '509 patent at col. 5:59-65).

In accordance with the definition above, Shichiri I discloses a "nonleachable glucose sensing enzyme." Shichiri I discloses that an glucose oxidase can be immobilized on a cellulose acetate film laminated to the surface of the front end 36 of the platinum electrode 34. (See

# EXHIBIT 10

PATENT
Docket No. 518852800100

+CERTIFICATE OF MAILING BY "EXPRESS MAIL"

Express Mail Label No.: EV 743883015 US Date of Deposit: February 1, 2006

I hereby certify that this paper or fee is being deposited with the United States Postal Service "Express Mail Post Office to Addressee" service under 37 C.F.R. § 1.10 on the date indicated above and is addressed to: Mail Stop Ex Parte Reexam, Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.

Cindy Guido

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In the Reexamination of:

James Say et al.

Patent No.: 6,175,752 B1

Issue Date: January 16, 2001

Issued To: TheraSense, Inc. (at issuance)

Examiner: To be assigned

**REQUEST FOR REEXAMINATION UNDER 37 C.F.R. § 1.510**

Mail Stop Ex Parte Reexam
Assistant Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Dear Sir:

On behalf of Dexcom, Inc. (hereafter "Requester"), the undersigned hereby submit under provisions of C.F.R. § 1.501 *et seq.*, a Request for Reexamination of claims 1-12, 14-35, 38-40, 42-45, 49-51, 53, 54, 58-65, 74-86, 88-90 and 92-94 of the above captioned U.S. Patent No. 6,175,752 to Say et al., entitled "ANALYTE MONITORING DEVICE AND METHODS OF USE," filed on April 30, 1998, and issued on January 16, 2001 (hereafter "the '752 patent"). The

'752 patent was originally assigned to TheraSense, Inc. ("Patentee"). This Request for Reexamination is based upon the following prior art references:

(1) EP Patent Application No. 83106571.9 to Shichiri et al., entitled "Portable Artificial Pancreas," filed July 5, 1983, published January 18, 1984 as EP publication no. 0098592 A2, citable under 35 U.S.C. §§ 102(a) and (b), and attached hereto as Exhibit 1 (hereinafter "Shichiri I");

(2) Shichiri et al., "Telemetry Glucose Monitoring Device With Needle-Type Glucose Sensor: A Useful Tool for Blood Glucose Monitoring in Diabetic Individuals," Diabetes Care, Vol. 9, No. 3, pp. 298-301, May-June 1986, citable under 35 U.S.C. §§ 102(a) and (b), and attached hereto as Exhibit 2 (hereinafter "Shichiri II");

(3) Ko et al., (Ed.), "Implantable Sensors for Closed-Loop Prosthetic Systems," Mount Kisco, NY: Futura Publishing Company, Inc., 1985, Chapter 15, entitled "Needle-type Glucose Sensor for Wearable Artificial Endocrine Pancreas," pp. 197-210, citable under 35 U.S.C. §§ 102(a) and (b), and attached hereto as Exhibit 3 (Shichiri III),

(4) U.S. Patent No. 5,569,186 to Lord et al., entitled "Closed Loop Infusion Pump System With Removable Glucose Sensor," filed April 25, 1994, issued October 29, 1996, citable under 35 U.S.C. §§ 102(a), (b) and (e), and attached hereto as Exhibit 4 (hereinafter "Lord I");

(5) U.S. Patent No. 4,494,950 to Fischell, entitled "Plural Module Medication Delivery System," filed January 19, 1982 and issued January 22, 1985, citable under 35 U.S.C. §§ 102(a), (b) and (e), and attached hereto as Exhibit 5 (hereinafter "Fischell");

(6) U.S. Patent No. 5,390,671 to Lord et al., entitled "Transcutaneous Sensor Insertion Set," filed March 15, 1994, issued February 21, 1995, citable under 35 U.S.C. §§ 102(a), (b) and (e), and attached hereto as Exhibit 6 (hereinafter "Lord II");

(7) PCT Application No. PCT/US96/02006 to Cheney et al., entitled "Transcutaneous Sensor Insertion Set," filed February 14, 1996, claiming priority to U.S. application no. 08/393,159, published on August 22, 1996 as WO 96/25089, citable under 35 U.S.C. §§ 102(a) and (b), and attached hereto as Exhibit 7 (hereinafter "Cheney");

(8) U.S. Patent No. 5,957,854 to Besson et al., entitled "Wireless Medical Diagnosis And Monitoring Equipment," filed December 5, 1997, claiming priority to PCT/EP94/02926, filed September 2, 1994 (now U.S. 5,862,803), citable under 35 U.S.C. §§ 102(a) and (e), and attached hereto as Exhibit 8 (hereinafter "Besson");

(9) U.S. Patent No. 6,219,574 to Cormier et al., entitled "Device And Method For Enhancing Transdermal Sampling," filed June 17, 1997, claiming priority to provisional application no. 60/019,990, filed June 18, 1996, issued on April 17, 2001, citable under 35 U.S.C. § 102(e), and attached hereto as Exhibit 9 (hereinafter "Cormier");

(10) U.S. Patent No. 4,703,756 to Gough et al., entitled "Complete Glucose Monitoring System With An Implantable Telemetered Sensor Module," filed May 6, 1986, issued November 3, 1987, citable under 35 U.S.C. §§ 102(a), (b) and (e), and attached hereto as Exhibit 10 (hereinafter "Gough");

(11) Stuart J. Updike et al., "Principles of Long-term Fully Implanted Sensors With Emphasis On Radiotelemetric Monitoring of Blood Glucose From Inside a Subcutaneous Foreign Body Capsule (FBC)," Biosensors in the Body: Continuous in vivo Monitoring, Chapter 4, pp. 117-137. © 1997 John Wiley & Sons Ltd, citable under 35 U.S.C. §§ 102(a) and (b) and attached hereto as Exhibit 11 (hereinafter "Updike");

(12) Mark C. Shults et al., "A Telemetry-Instrumentation System for Monitoring Multiple Subcutaneously Implanted Glucose Sensors," IEEE Transactions On Biomedical Engineering, Vol. 41, No. 10, pp. 937-942, October 1994. © 1994 IEEE, citable under 35 U.S.C. §§ 102(a) and (b), and attached hereto as Exhibit 12 (hereinafter "Shults");

(13) Brian D. McKean et al. "A Telemetry-Instrumentation System for Chronically Implanted Glucose and Oxygen Sensors," IEEE Transactions On Biomedical Engineering, Vol. 35, No. 7, © July 1988 IEEE, citable under 35 U.S.C. §§ 102(a) and (b), and attached hereto as Exhibit 13 (hereinafter "McKean");

(14) Jon C. Armour et al., "Application of Chronic Intravascular Blood Glucose Sensor in Dogs," Diabetes, Vol. 39, December 1990, citable under 35 U.S.C. §§ 102(a) and (b), and attached hereto as Exhibit 14 (hereinafter "Armour");

(15) Michael Thompson et al., "*In Vivo* Probes: Problems and Perspectives," Clinical Biochemistry, Vol. 19, October 1986, citable under 35 U.S.C. §§ 102(a) and (b), and attached hereto as Exhibit 15 (hereinafter "Thompson");

(16) G. Velho et al., "Strategies for calibrating a subcutaneous glucose sensor," Biomed. Biochim. Acta 48 (1989) (presented at the International Workshop on Intracorporal Glucose Sensors," September 27-30, 1988, Göhren-Lebbin, GDR), citable under 35 U.S.C. §§ 102(a) and (b), and attached hereto as Exhibit 16 (hereinafter "Velho");

(17) European Patent Application No. 90302932.0 to Skotheim et al., entitled "Electrochemical biosensor based on immobilized enzymes and redox polymers," filed on March 19, 1990, published as EP 0 390 390 A1 on October 3, 1990, citable under 35 U.S.C. §§ 102(a) and (b), and attached hereto as Exhibit 17 (hereinafter "Skotheim");

(18) U.S. Patent No. 4,538,616 to Rogoff entitled "Blood Sugar Level Sensing and Monitoring Transducer," filed on July 25, 1983, issued on September 3, 1985, citable under 35 U.S.C. §§ 102(a), (b) and (e), and attached hereto as Exhibit 18 (hereinafter "Rogoff").

Pursuant to 35 U.S.C. § 303, Requester submits that the above-listed prior art references raise "substantial new questions of patentability" with respect to at least claims 1-12, 14-35, 38-40, 42-45, 49-51, 53, 54, 58-65, 74-86, 88-90 and 92-94 of the '752 patent. As required by 37 C.F.R. § 1.510(b)(1), a statement pointing out each substantial new question of patentability is

provided below for each identified claim for which reexamination is requested. Furthermore, a detailed explanation of the pertinence and manner of applying the cited patents and publications to each identified claim is provided pursuant to 37 C.F.R. § 1.510(b)(2). As required by 37 C.F.R. §§ 1.510(b)(3) and 1.510(b)(4), copies of the pertinent patents and publications relied upon, and a copy of the entire '752 patent including the front face, drawings, specification and claims (in double column format) are included. The fee for requesting reexamination under 37 C.F.R. 1.20(c) is also enclosed.

## I. Introduction

Generally, the '752 patent is directed to an analyte monitoring device that includes a transcutaneous electrochemical sensor, a sensor control unit and a display unit configured to receive radio frequency (radio) signals from the sensor control unit. The sensor control unit has a housing adapted for placement on a patient's skin and adapted to receive a portion of an electrochemical sensor. The sensor control unit also includes two or more conductive contacts disposed on the housing and configured for coupling to two or more contact pads on the electrochemical sensor. A transmitter is disposed in the housing of the sensor control unit and coupled to the plurality of conductive contacts for transmitting data obtained by the electrochemical sensor. As described in further detail below, however, prior art devices and systems taught each of the various embodiments of the purported invention recited in the identified claims of the '752 patent for which reexamination is requested. Because the prior art references disclose and teach each and every element of the identified claims, each of these claims are anticipated and/or rendered obvious by the prior art references.

It is noted that in the context of reexamining patent claims, "the PTO must apply the broadest reasonable meaning to the claim language, taking into account any definitions presented in the specification. *In re Bass*, 314 F.3d 575, 577 (Fed. Cir. 2002) (citing *In re Yamamoto*, 740 F.2d 1569, 1571 (Fed. Cir. 1984). Giving claims their broadest reasonable construction "serves

# EXHIBIT 11

(1) M. Sakakida, et al., "Ferrocene-mediated Needle-type Glucose Sensor Covered with Newly Designed Biocompatible Membrane," *Sensors and Actuators B*, vol. 13-14, 319-322 (1993), published as the May-June 1993 volume, citable under 35 U.S.C. §§ 102(a) and (b), and attached hereto as Exhibit 1 (hereinafter "Sakakida");

(2) M. Shichiri, et al., "Needle-type Glucose Sensor for Wearable Artificial Endocrine Pancreas," Chapter 15 in IMPLANTABLE SENSORS FOR CLOSED-LOOP PROSTHETIC SYSTEMS, W. H. Ko, ed., Futura Publishing Co., Mount Kisco, NY (1985), citable under 35 U.S.C. §§ 102(a) and (b), and attached hereto as Exhibit 2 (hereinafter "Shichiri");

(3) G. S. Wilson, et al., "Progress Toward the Development of an Implantable Glucose Sensor," G. S. Wilson, et al., *Clinical Chemistry*, vol. 38(9), 1613-17 (1992), citable under 35 U.S.C. §§ 102(a) and (b), and attached hereto as Exhibit 3 (hereinafter "Wilson Clinical Chemistry");

(4) U.S. Patent No. 5,165,407 to Wilson, et al., entitled "Implantable Glucose Sensor," filed on April 9, 1991, issued on November 24, 1992, citable under 35 U.S.C. §§ 102(a), (b) and (e), and attached hereto as Exhibit 4 (hereinafter "Wilson '407 patent");

(5) U.S. Patent No. 5,322,063 to Allen, et al., entitled "Hydrophilic Polyurethane Membranes for Electrochemical Glucose Sensors," filed on October 4, 1991, issued on June 21, 1994, citable under 35 U.S.C. § 35 U.S.C. §§ 102(a), (b), and (e), and attached hereto as Exhibit 5 (hereinafter "Allen");

(6) Shichiri et al., "Membrane Design for Extending the Long Life of an Implantable Glucose Sensor," *Diab. Nutr. Metab.*, vol. 2(4), 309-313 (1989), published in 1989, citable under 35 U.S.C. §§ 102(a) and (b), and attached hereto as Exhibit 6 (hereinafter "Shichiri '89");

(7) Johnson, et al., "Techniques to Improve the Performance of Electrochemical Sensors," U.S. Patent No. 5,411,647; issued on May 2, 1995, filed on January 25, 1994 as a

continuation of Ser. No. 980,465, filed on November 23, 1992, now abandoned; citable under 35 U.S.C. §§ 102(a) and (e), and attached hereto as Exhibit 7 (hereinafter "Johnson"); and

(8) Wilkins, "In Vivo Refillable Glucose Sensor," U.S. Patent No. 4,986,271, filed July 19, 1989 and issued January 22, 1991, citable under 35 U.S.C. §§ 102(a), (b) and (e), and attached hereto as Exhibit 8 (hereinafter "Wilkins").

Pursuant to 35 U.S.C. § 303, Requester submits that the above-listed prior art references raise "substantial new questions of patentability" with respect to at least claims 1-10, 16-20, 22, 25-43, 47 and 48 of the '161 patent. As required by 37 C.F.R. § 1.510(b)(1), a statement pointing out each substantial new question of patentability is provided below for each claim for which reexamination is requested. Furthermore, a detailed explanation of the pertinence and manner of applying the cited patents and publications to each identified claim is provided pursuant to 37 C.F.R. § 1.510(b)(2). As required by 37 C.F.R. §§ 1.510(b)(3) and 1.510(b)(4), copies of the pertinent patents and publications relied upon, and a copy of the entire '161 patent including the front face, drawings, and specification/claims (in double column format) are included. The fee for requesting reexamination under 37 C.F.R. 1.20(c) is also enclosed.

## I. Introduction

### A. The '161 Patent in the *Abbott v. DexCom* Litigation

The '161 patent is presently involved in litigation. Therefore, Requester and the undersigned respectfully request that the present reexamination proceeding be conducted with "special dispatch" as having priority over all other cases pursuant to 35 U.S.C. § 305 and MPEP § 2261.

On August 11, 2005, Abbott Diabetes Care, Inc. filed a Complaint (Exhibit 9) against DexCom, Inc. in the United States District Court for the District of Delaware. Abbott's

# EXHIBIT 12

PATENT
Docket No. 518852800200

CERTIFICATE OF MAILING BY "EXPRESS MAIL"

Express Mail Label No.: EV 761644961 US Date of Deposit: February 1, 2006

I hereby certify that this paper or fee is being deposited with the United States Postal Service "Express Mail Post Office to Addressee" service under 37 C.F.R. § 1.10 on the date indicated above and is addressed to: Mail Stop Ex Parte Reexam, Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.

Diane Blevins

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In the Reexamination of:

Adam Heller, et al.

Patent No.: 6,284,478 B1

Issue Date: September 4, 2001

Assignee: TheraSense, Inc. (at issuance)

Examiner: To be assigned

**REQUEST FOR REEXAMINATION UNDER 37 C.F.R. § 1.510**

Mail Stop Ex Parte Reexam
Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Dear Sir:

On behalf of DexCom, Inc. (hereafter "Requester"), the undersigned hereby submit under provisions of C.F.R. §§ 1.501, *et seq.*, a Request for Reexamination of claims 1-3, 9, 13, 16, 18-20, 23, 24, 26-29, 32, 33, 35, 52-57, 59, 61 and 73 of above captioned U.S. Patent No. 6,284,478 to Heller, et al., entitled "SUBCUTANEOUS GLUCOSE ELECTRODE," filed on December 4, 1996, and issued on September 4, 2001 (hereinafter "'478 patent"). The '478 patent was assigned to TheraSense, Inc. ("TheraSense") at issuance and is currently assigned to Abbott Laboratories.

This Request for Reexamination is based upon the following prior art references:

(1) M. Sakakida, *et al.*, "Ferrocene-mediated Needle-type Glucose Sensor Covered with Newly Designed Biocompatible Membrane," *Sensors and Actuators B*, vol. 13-14, 319-322 (1993), published as the May-June 1993 volume, citable under 35 U.S.C. §§ 102(a) and (b), and attached hereto as Exhibit 1 (hereinafter "Sakakida");

(2) Sakakida, *et al.*, *Artif. Organs Today*, 2(2):145-158 (1992), published in 1992, citable under 35 U.S.C. §§ 102(a) and (b), and attached hereto as Exhibit 2 (hereinafter "Sakakida '92");

(3) Shichiri, *et al.*, "Membrane Design for Extending the Long-Life of an Implantable Glucose Sensor," *Diab. Nutr. Metab.*, 2:309-313 (1989), citable under 35 U.S.C. §§ 102(a) and (b), and attached hereto as Exhibit 3 (hereinafter "Shichiri '89");

(4) R. Sternberg, *et al.*, "Study and Development of Multilayer Needle-type Enzyme-based Glucose Microsensors," *Biosensors* vol. 4, 27-40 (1988), citable under 35 U.S.C. §§ 102(a) and (b), and attached hereto as Exhibit 4 (hereinafter "Sternberg"); and

(5) Wilkins, "*In Vivo* Refillable Glucose Sensor," U.S. Patent No. 4,986,271, filed July 19, 1989 and issued January 22, 1991, citable under 35 U.S.C. §§ 102(a), (b) and (e), and attached hereto as Exhibit 5 (hereinafter "Wilkins").

Pursuant to 35 U.S.C. § 303, Requester submits that the above-listed prior art references raise "substantial new questions of patentability" with respect to at least claims 1-3, 9, 13, 16, 18-20, 23, 24, 26-29, 32, 33, 35, 52-57, 59, 61 and 73 of the '478 patent. As required by 37 C.F.R. § 1.510(b)(1), a statement pointing out each substantial new question of patentability is provided below for each claim for which reexamination is requested. Furthermore, a detailed explanation of the pertinence and manner of applying the cited patents and publications to each identified claim is provided pursuant to 37 C.F.R. § 1.510(b)(2). As required by 37 C.F.R. §§ 1.510(b)(3) and 1.510(b)(4), copies of the pertinent patents and publications relied upon, and

# EXHIBIT 13

FILED UNDER SEAL